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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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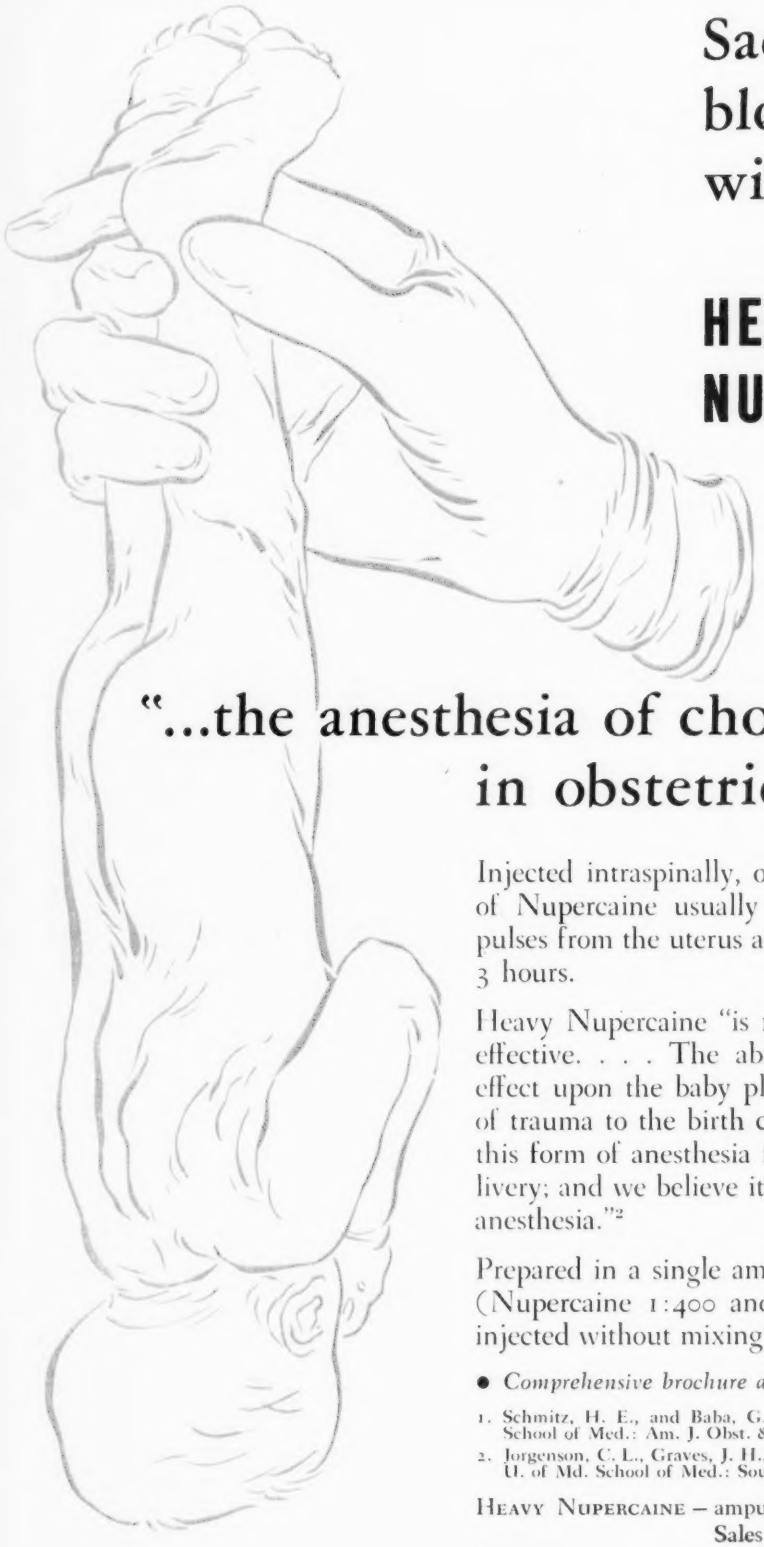

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2. Jorgenson, C. L., Graves, J. H., and Savage, J. E., Dept. of Obst., U. of Md. School of Med.: Southern Med. J., Sept., 1948.

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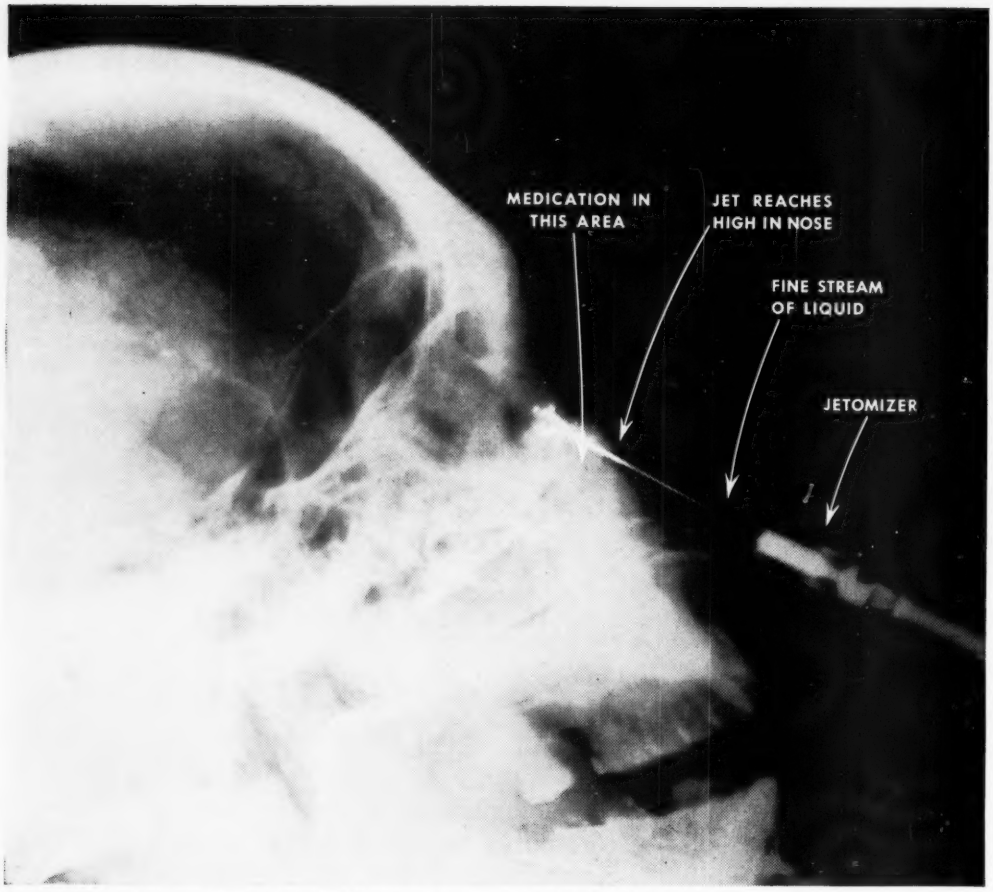

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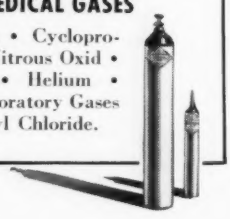

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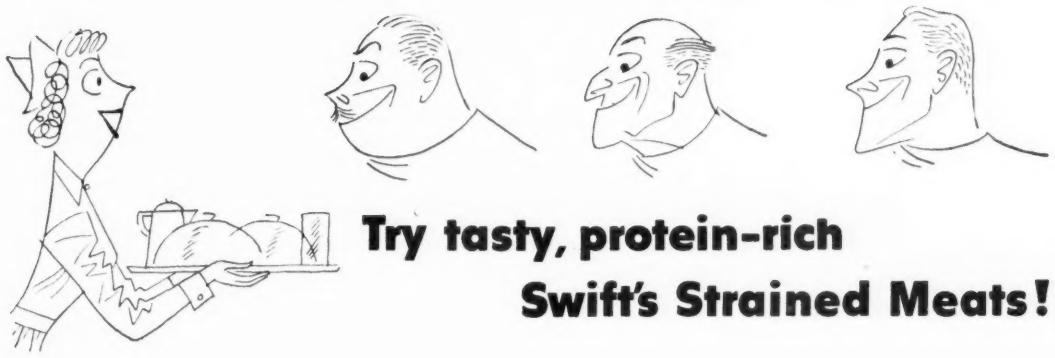

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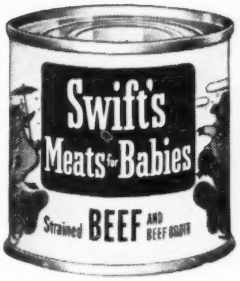

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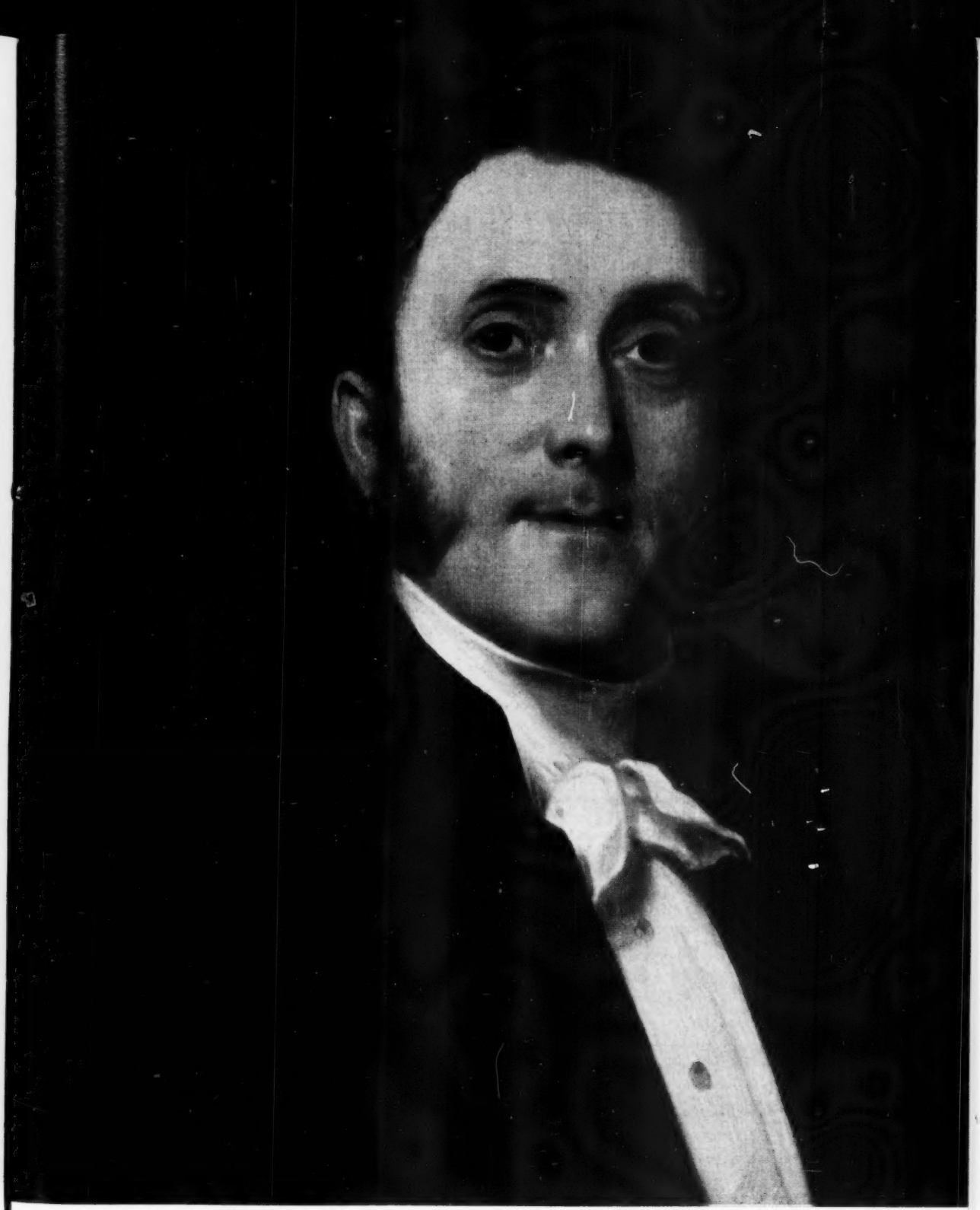

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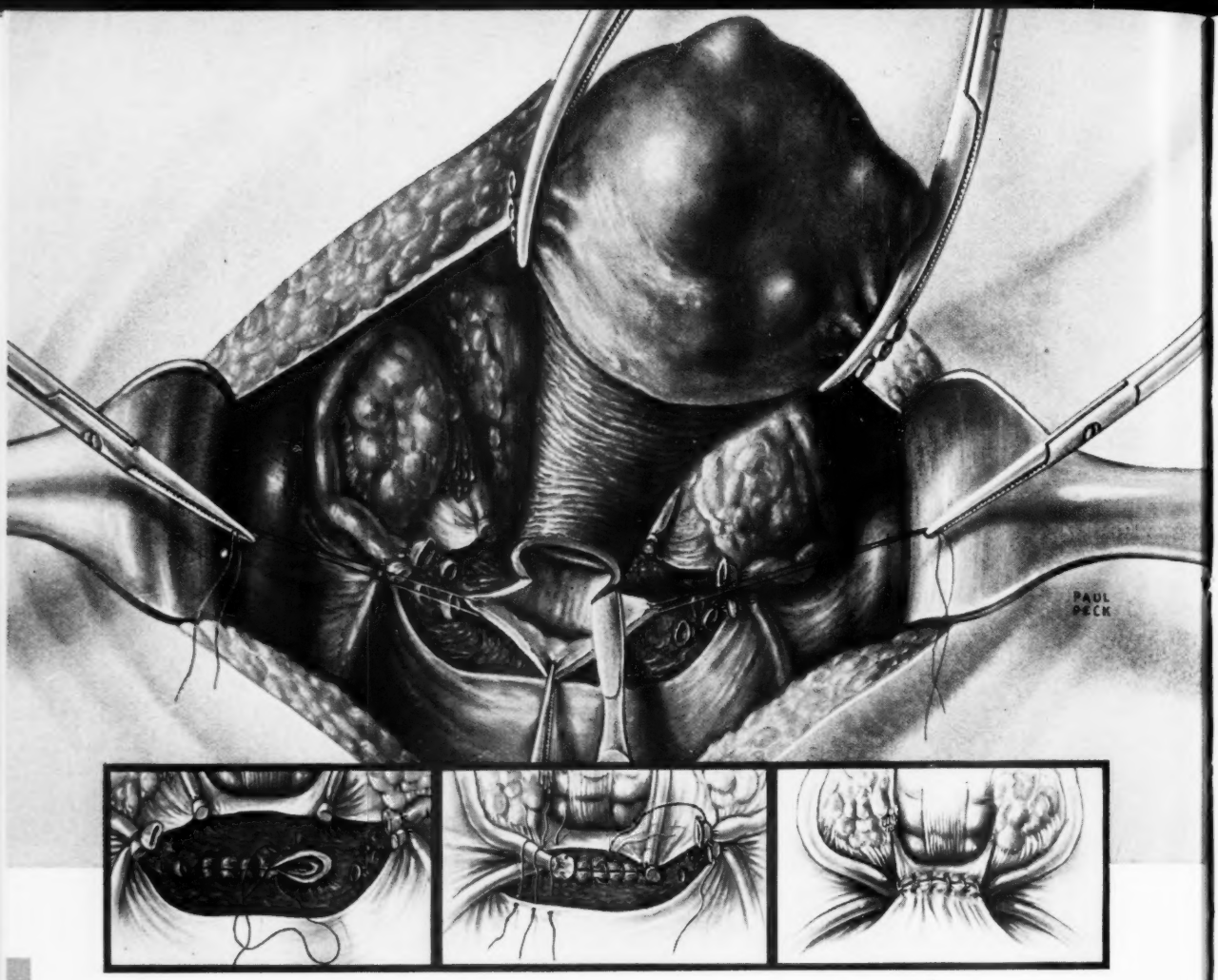

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The clumsy bulk of the eyed needle, combined with the doubled strand, with its attendant tearing or ripping of tissue, has influenced the more meticulous technicians to take advantage of the refinements derived from the eyeless needle.

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The eyed needle does greater injury to tissue because it pulls a looped suture in its wake. The eyeless needle causes minimal trauma by pulling a single strand, slightly smaller than the needle.

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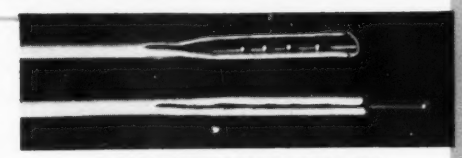
As shown, the swage has no seam. The suture is inserted in a bored aperture in high-tempered steel, then locked by compression. No rough edges or gaps to scrape tissue. This new swage is only one-quarter as long as the conventional swage, yet tests show superior holding power.



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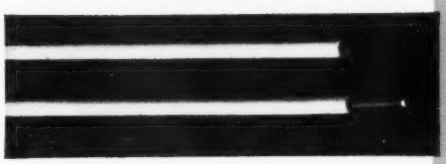

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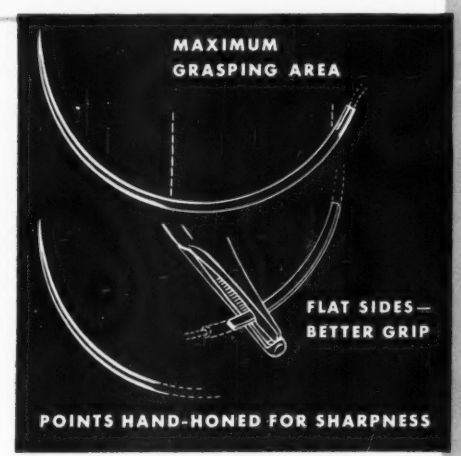

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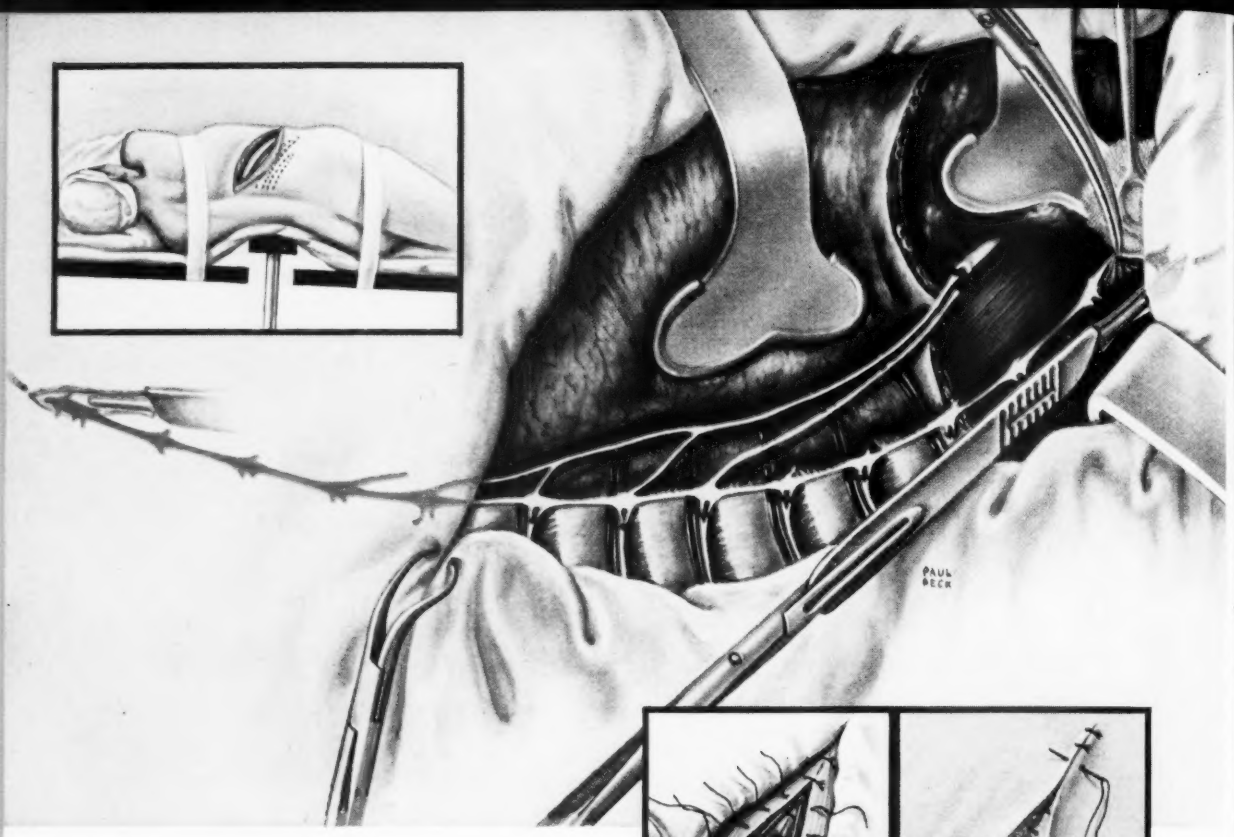

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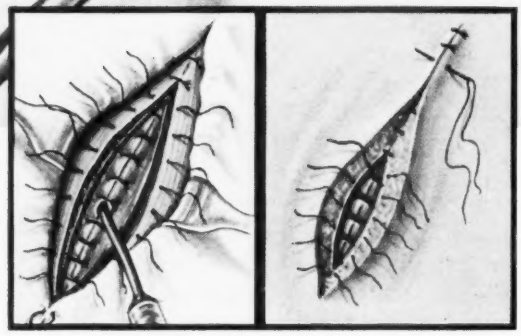

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*Beams, A. J., and Endicott, E. T., Histologic changes in the livers of patients with cirrhosis treated with methionine, Gastroenterology 9:718-735 (Dec.) 1947.

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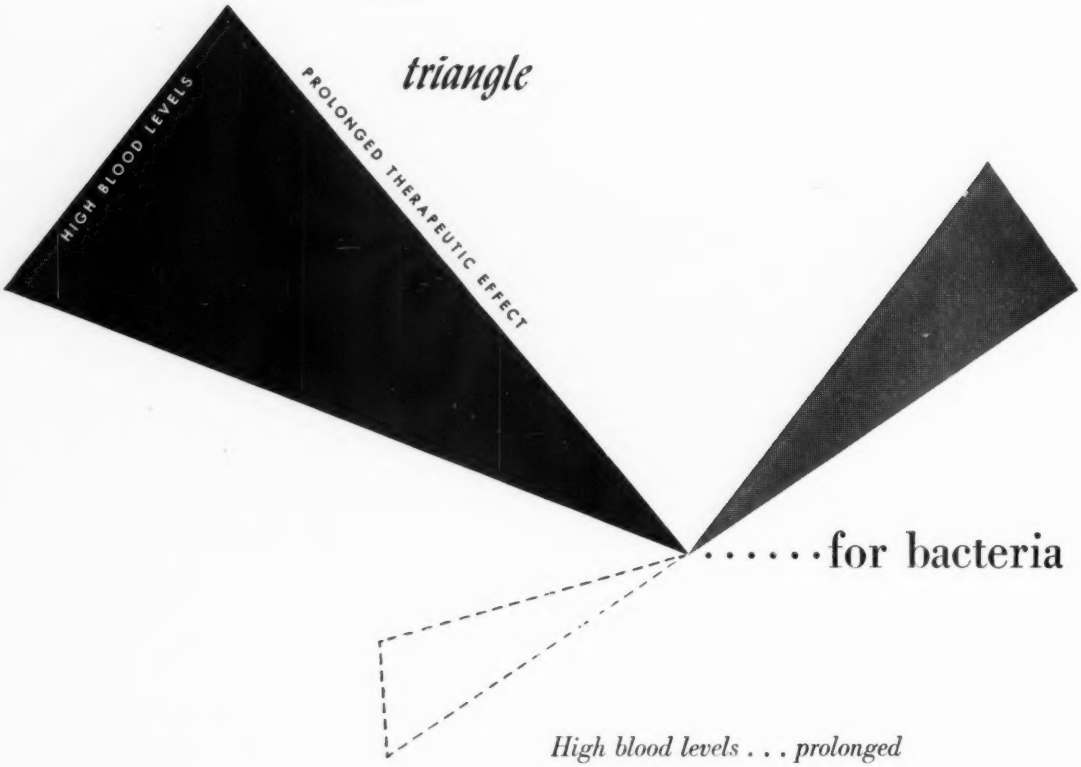

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SURGERY

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Original Communications

THE INFLUENCE OF PREGNANCY ON CANCER OF THE BREAST

BARNEY BROOKS, M.D., AND JAMES N. PROFFITT, M.D., NASHVILLE, TENN.

(From the Department of Surgery, Vanderbilt University School of Medicine)

THE stimulus for the investigation which forms the basis of this paper came from a series of incidents briefly summarized as follows:

1. On Feb. 3, 1947, a patient, childless, aged 35 years, was subjected to a radical operation on one breast for carcinoma. During the course of the operation and from examination of the specimen removed, there was no evidence of the tumor having extended outside the limits of the mammary gland. The patient was very desirous of having a child and neither sterilization nor contraceptive measures were advised.

2. She subsequently moved to another state and when she was six months pregnant came to the attention of a surgeon there who wrote the senior author as follows:

"According to the patient's story she has had a radical removal of one breast for cancer and has been told it would be perfectly all right for her to become pregnant. This is so in variance from our experience here that I would certainly appreciate it if you would let me know if you or your group there have any recent information on this subject."

3. At the time this communication was received another patient, operated upon by the senior author at the age of 28 years for carcinoma of the breast without demonstrable extension of the tumor outside the mammary gland, was in the Vanderbilt Hospital, two years after operation, having just been delivered of a normal child.

The purpose of this investigation was to determine facts recorded in the literature and from our own experience in the Vanderbilt Hospital during the past twenty-two years, in which there has been a particular interest in cancer of the breast, not only in the surgical pathologic laboratory for the determination of the extent of the disease, but from various members of the staff having been interested in the follow-up of these patients so that the result of almost every patient operated on during this period is known.

Our practice has been based on the opinion that although pregnancy exerted a marked influence on existing cancer originating in the mammary gland, it was not influential in the production of cancer in this gland. We have, therefore,

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not urged a patient to avoid pregnancy if we had reasonable grounds for a belief that all tumor cells were removed. We have, however, advised sterilization or use of contraceptives in patients whom we felt comparatively certain were not permanently cured and more recently we have attempted to give the patient an understanding of the possible deleterious effect of pregnancy on existing cancer of the breast in order that she might have an opportunity of herself choosing between living a year longer with no child or a year less and realize a necessarily fundamental longing.

From reason alone it would appear that the acceptance of the truth of any or all theories for the cause of cancer as yet proposed would make it impossible to escape the conclusion that the frequency of neoplastic disease in any organ would be increased by the addition of a specific stimulus producing cell division in this organ. The mammary gland of the female is unique not only because of frequently repeated anatomic and physiologic changes, but because of the magnitude of these changes.

In a previous communication, Brooks and Daniel[1] pointed out the desirability of any investigator of the final result of a so-called radical operation for cancer of the breast recognizing the fact that the techniques employed in this operation varied considerably in different surgical clinics and even as employed by individual surgeons in the same surgical clinic. With very few exceptions, none of which could in any way influence the conclusions reached in this study, radical operations for breast cancer in the Vanderbilt Hospital have been performed by the same technique. Palliative operations or biopsies have been done in such patients as were deemed inoperable. The technique used was described in a previous communication by Brooks and Daniel.[1] In brief, it is a bloc dissection in which the margins of the bloc are made with a sharp knife and stripping by gauze is not employed for the removal of the contents of the axilla. The bloc removed consists of an area of skin so large as to require skin transplantation together with the axillary contents to the level of the axillary vessels, the mammary gland, the subcutaneous fat, the fascia and muscles bounded by the clavicle, the midline and the anterior margin of the latissimus dorsi muscle, including the fascia of the first segment of the rectus abdominis muscle.

From Oct. 1, 1925, to Jan. 1, 1948, there have been 395 patients operated on, in one way or another, at the Vanderbilt University Hospital for cancer of the breast. Of these, 123 were less than 46 years old and were arbitrarily considered in the childbearing age and constitute the basis of this paper. The present condition of all of these patients is known; 70 have been operated upon for more than five years and 44 for less than five years (Tables I and II). In 6 patients carcinoma was present during pregnancy or lactation (Table III). In 5 patients pregnancy occurred after radical operation was performed on one breast (Table IV). It is interesting and perhaps significant, but unfortunate for reaching any definitely reliable conclusion that, from 1925 to 1930, there was no instance of carcinoma of the breast in which pregnancy or lactation was concomitant with the neoplasm or occurred subsequent to its radical removal. Five of the six instances of carcinoma of the breast occurring during pregnancy or lactation were in patients admitted to the Vanderbilt Hospital between 1932 and 1939. The sixth patient was not seen until 1946. All patients becoming

TABLE I. ALL PATIENTS UNDER 46 YEARS OF AGE WITH ANY OPERATION IN VANDERBILT HOSPITAL FOR CARCINOMA OF MAMMARY GLAND

	OPERATED ON 5 YR. OR MORE						OPERATED ON LESS THAN 5 YR.					
	ALIVE		DEAD		TOTAL		ALIVE		DEAD		TOTAL	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Radical amputations of breast	29	46	34	54	63	80	23	60	15	40	38	86
1. With axillary metastases	12*	30	28	70	40		8	36	14	64	22	
2. Without axillary metastases	17†	74	6	26	23		15	93	1	7	16	
Simple mastectomies with axillary metastases or ulceration	1	8	11	92	12	15	3	60	2	40	5	11
Biopsies (for diagnosis)	0		4	100	4	5	0		1		1	3
Total carcinomas of breast	30	38	49	62	79		26	59	18	41	44	

*Two patients listed as "alive" are dead from causes other than recurrence of carcinoma. One died in another hospital from a cerebral accident sixteen years after operation. Another died of cirrhosis of the liver of many years' duration (five years after radical mastectomy).

Two other patients are alive but have distant metastases at this time.

†One patient listed as "alive" died eight years after radical mastectomy with primary bronchiogenic carcinoma.

TABLE II. PATIENTS UNDER 46 YEARS OF AGE OPERATED UPON FOR CARCINOMA OF THE BREAST AT THE VANDERBILT UNIVERSITY HOSPITAL AND OBSERVED FOR FIVE YEARS OR MORE AFTER OPERATION

	NUMBER OF CASES	NUMBER PATIENTS LIVING 5 YR. AFTER OPERATION	NUMBER PATIENTS DEAD WITH RECURRENCE IN 5 YR.	PER CENT LIVING 5 YR. OR LONGER	NUMBER PATIENTS WHO LIVED OVER 5 YR. BUT DIED WITH RECURRENCE	TOTAL PER CENT APPARENTLY "CURED"
Group I. No axillary metastases	22	17*	5	77	1	73
Group II (microscopic metastases)	4	4	0	100	2	50
Group III (gross axillary metastases)	41	12	29	29	3†	22
Group IV (distant metastases)	6	0	6	0	0	0
Patient pregnant after operation (no axillary metastases)	1	1	0	100	0	100
Patients pregnant or lactating at time tumor discovered (all had gross axillary metastases)	5‡	1	4	20	0	20
Total	79	35	44	44	6	38

*One patient listed as "alive" died eight years after radical mastectomy with primary bronchiogenic carcinoma.

†Two additional patients have distant metastases but are not yet dead.

‡Three patients had a simple mastectomy.

TABLE III. PATIENTS PREGNANT OR LACTATING WHEN TUMOR DISCOVERED

S.P. NO.	AGE (YR.)	DATE TUMOR DISCOVERED	PREGNANT OR LACTATING WHEN TUMOR FOUND	PATHOLOGIC TYPE OF TUMOR	OPERATION PERFORMED	DATE OF OPERATION	ADDITIONAL TREATMENT	FOLLOW-UP	REMARKS
4087	33	4 mo. prior to admission (1 mo. prior to delivery)	Pregnant	Adenocarcinoma with axillary metastases	Radical mastectomy	6/ 3/32	X-ray preoperative and postoperative (no x-ray castration)	Patient living and well 15½ yr. later	Viable child delivered 3 mo. prior to admission
4196	32	Ulceration nipple 4 yr. prior to admission; tumor 8 mo. prior to admission	Pregnant	Paget's disease adenocarcinoma with axillary metastases	Simple mastectomy (ulceration of breast)	7/15/32	Postoperative x-ray therapy	Died 5/10/33	8 mo. pregnant when admitted; labor induced, delivered viable child 7/3/32
7471	36	2 yr. prior to admission	Lactating when tumor discovered; 3 mo. pregnant at operation	Adenocarcinoma with axillary metastases	Simple mastectomy (ulceration of breast)	1/13/35	Postoperative x-ray to breast and axilla	Pulmonary metastases 9/23/36; died 1/26/37 (6 mo. after delivery)	Delivered full-term viable child
8164	39	2 mo. prior to admission	Lactating	Carcinoma (undifferentiated) with axillary metastases	Simple mastectomy (ulceration of breast)	9/18/36	Postoperative x-ray therapy	Pulmonary metastases Feb., 1937; died April, 1937	
9357	30	Tumor of breast for 5 mo.; weakness and anemia for 6 mo.	Pregnant	Adenocarcinoma of breast with axillary metastases; metastases to bone	1. Biopsy axillary lymph node 2. Radical mastectomy 3. Sternal biopsy	1. 10/ 7/37 2. 1/26/38 3. 7/12/38	X-ray castration March, 1938	Improved after delivery; began to lose strength in June, 1938; died 12/8/38	Cesarean section 11/16/37, viable child; bone lesions improved by 1/14/38
20933	21	11 mo. prior to admission	Lactating	Duct carcinoma with axillary metastases	Simple mastectomy ("inflammatory carcinoma")	10/31/46	X-ray castration, x-ray therapy to axilla and supraclavicular regions; testosterone proprinate 50 mg. weekly	Died 1/19/48	

TABLE IV. PATIENTS PREGNANT AFTER RADICAL AMPUTATION OF BREAST FOR CARCINOMA

CASE S.P.NO.	AGE AT OPERATION (YR.)	DATE OF OPERATION	PREGNANCIES	PATHOLOGIC TYPE OF TUMOR	FOLLOW-UP	LIVING CHILDREN AT TIME OF OPERATION	REMARKS
13730	24	4/ 4/41	1. Abortion of 3 mo. fetus 15 mo. P.O. 2. Normal delivery 3 yr. P.O.	Duct carcinoma; no axillary metastases	No recurrence	2	Some difference of opinion as to whether this lesion was malignant
18932	31	5/ 4/45	Normal delivery 1 yr P.O. 5/14/46	Adenocarcinoma with gross axillary metastases	Died 7/21/46	2	Advised against pregnancy
18935	28	5/ 5/45	1. Normal delivery 2 yr. P.O.	Adenocarcinoma; no axillary metastases	No recurrence	0	
20119	35	4/24/46	Pregnant at present time	Duct carcinoma; no axillary metastases	No recurrence	2	
21310	35	2/ 3/47	Normal delivery 1 yr P.O.	Duct carcinoma; no axillary metastases	No recurrence	0	

pregnant subsequent to a radical mastectomy for carcinoma have been observed since 1940 and only one of these patients has been observed for more than five years after operation.

Examination of Table I reveals that of the 79 patients under 46 years of age with carcinoma of the breast who have been followed five years or more after operation, 30 (38 per cent) were alive at the end of five years or more, and 49 (62 per cent) died from carcinoma. Of all patients seen, 63 (80 per cent) were deemed operable and had radical amputation of the breast. Of this group 40 had either gross or microscopic axillary metastases, and 23 had no gross or microscopic evidence of axillary metastases. In 40 patients with axillary metastases only 12 (30 per cent) were alive after five years and two of these had unmistakable evidence of recurrence of carcinoma. Two of the 12 patients listed as "alive" died from causes other than cancer at sixteen years, and five years, respectively, after radical mastectomy. Autopsy was not done on either but there was no clinical evidence of recurrence at the time of death. Of the 23 patients without gross or microscopic evidence of axillary metastases, 17 (74 per cent) lived five or more years after operation. One of these patients listed as "alive" died eight years after operation from what was shown at autopsy to be primary bronchiogenic carcinoma. There was no evidence of recurrence of the carcinoma of the breast. When first seen, 12 patients had such extensive axillary metastases or ulceration of the breast that a simple mastectomy was carried out. Only one of these is alive after five years. In 4 patients the carcinoma was so extensive that only a biopsy was done for diagnosis prior to x-ray therapy. These all died from carcinoma.

Examination of the women under 46 years of age operated upon for carcinoma of the breast at the Vanderbilt University Hospital and observed for five

years or more after operation is interesting when arranged according to pathologic groups (Table II). There were 22 patients with no gross or microscopic evidence of axillary metastases. All of these had radical mastectomy. Of these, 17 (77 per cent) survived operation five years, however, 1 patient died from recurrence of carcinoma more than five years after operation. None of the remaining 16 patients have any evidence of recurrence of carcinoma.

In the 4 patients with only microscopic evidence of axillary metastases all were subjected to radical mastectomy and all lived five years but 2 died later from recurrence of carcinoma.

The largest group of patients, 41, had gross evidence of carcinoma in the axillary lymph nodes. Seven of the patients had simple mastectomies because of ulceration of the breast. The remaining 34 had radical mastectomies. Only 12 (29 per cent) patients survived operation five years. One died more than five years after operation and 2 patients who have survived operation more than five years have distant metastases at this time. Of 41 patients with gross axillary metastases only 9 (22 per cent) appear "cured."

Six patients had distant metastases when first observed. Two of these had a simple mastectomy and 4 had biopsy for diagnosis. None of this group survived five years.

Only 1 patient has been pregnant subsequent to radical mastectomy for carcinoma of the breast and subsequently followed five years. This patient (S. P. 13730, Table IV) had no axillary metastases and there was some difference among pathologists as to whether this lesion was actually carcinoma.

Five women (Tables II and III) who were pregnant or lactating when the carcinoma was discovered, have been followed five years or more. Two of these patients had a radical mastectomy and 3 had a simple mastectomy. One additional patient is included (S. P. 20933) who has not been followed five years but the outcome is already known. These patients ranged in age from 21 years to 39 years. Three were pregnant at the time the tumor was discovered and 3 were lactating. All had gross axillary metastases, and all except 1 were dead in two years from the time first observed. Geschickter[2] could find no report of a cure of carcinoma of the breast operated on during pregnancy.

CASE REPORTS

The patient who is alive would appear to be the "proverbial exception to prove the rule." The following is an account of one case.

This white patient, when she was 33 years old and eight months pregnant, noted a hard, painless lump in the breast. Four months later, after normal delivery, she was admitted to the Vanderbilt Hospital* where immediate x-ray therapy was instituted and operative treatment was postponed for a period of two weeks for the purpose of ending lactation. A radical mastectomy was performed and pathologic examination showed the neoplasm to be an adenocarcinoma with axillary metastases. This patient is alive and well 15½ years after operation. Menses are now becoming irregular and her only complaints are menopausal in origin.

Parenthetically, one cannot resist the temptation to call attention to the effect the inclusion of this patient would have in determining *average* duration of life in this group of patients.

*As a patient of Dr. W. A. Bryan.

One of the patients dying within two years is of particular importance to the subject of this paper.

This (S. P. 9357, Table III) was a 30-year-old white woman admitted on the medical service, Oct. 2, 1937, because of weakness and anemia of six months' duration. She had noticed a painless "lump" in the left breast for five months prior to admission. Examination revealed an extremely emaciated white woman, obviously very anemic who had generalized glandular enlargement, with some enlargement of the spleen. An egg-sized hard mass lay beneath the left nipple attached to the skin. Hard, enlarged lymph nodes were felt in the left axilla. In addition, she was found to be seven months pregnant. Red blood cell count was 2.05 million with 5.9 Gm. of hemoglobin. The white count was 33,000 with 25 per cent lymphocytes, 10 per cent segmented and 41 per cent unsegmented polymorphonuclear leucocytes, 1 per cent monocytes, and 23 per cent unclassified cells. Serum Ca was 9.8 mg. per cent. Serum PO_4 was 2.58 mg. per cent. The medical diagnosis was myelogenous leucemia. A surgical consultant saw the patient and thought the entire picture could be explained by carcinoma of the breast with diffuse bone metastases. Biopsy of left axillary lymph node revealed adenocarcinoma in the node. X-ray of the skull, ribs, pelvis, lumbar spine, and dorsal spine revealed innumerable areas of increased penetration of x-rays through the bones, thought to be due to metastatic carcinoma. She received numerous blood transfusions. The white blood cell count fell gradually to 9,800 per cubic millimeter. On Nov. 16, 1937, a cesarean section was done and a viable child obtained. The patient was not allowed to nurse the child. There was an uneventful recovery after operation. When she returned to the hospital Jan. 19, 1938, she presented an entirely different, and strikingly remarkable change. She had gained weight and appeared in excellent health. The mass in the left breast was then difficult to feel. X-ray examination revealed remarkable disappearance of the bone destruction previously seen (Fig. 1, *A*, *B*, *C*, and *D*). A radical amputation of the left breast was done Jan. 25, 1938. Adenocarcinoma of the breast was found with gross axillary metastases. She did well postoperatively. However, x-ray views in June, 1938, revealed an increase in the bone destruction. In July, 1938, a sternal bone marrow biopsy was done and carcinoma was found in the bone marrow. She went steadily downhill. The x-ray pictures revealed ever-increasing bone destruction. The liver and spleen grew increasingly large. She died Dec. 8, 1938, and autopsy revealed metastases to liver, spleen, lungs, vertebra, skull, ribs, meninges, right breast, and gall bladder.

From this group of patients it would appear as if the one patient now living 15½ years after operation for a cancer of the breast would have to be considered as having had all tumor cells removed and since the tumor was observed only one month before the termination of pregnancy, and lactation was terminated only two weeks before radical operation, there was not adequate time for a demonstrable effect of either pregnancy or cessation of lactation. There was, however, a period of three months of lactation during which time the patient noted an increase in size of the lump in the breast, but it would be folly to speculate as to whether or not axillary metastases occurred during this period. The other five patients all having died within a period of two years, certainly supports previously expressed opinion that pregnancy promotes the rapidity of growth of an existing cancer of the mammary gland.

Observation of patients pregnant after radical amputation of breast for carcinoma (Table IV) reveals no instance of primary or recurrent cancer in the remaining breast after radical operation for breast cancer. We are well aware that only one of these patients has been observed for a period in excess of five years and that one of them is still pregnant. In two patients, enough time has elapsed since the termination of pregnancy that any subsequent appearance of a tumor could hardly be attributed to pregnancy. The only patient who is dead was advised against pregnancy, because she had gross axillary metastases and

consequently only a 30 per cent chance of having had all the tumor removed by radical mastectomy.

As to the influence of pregnancy on the causation of cancer of the mammary gland, there are no existing data from which reliable conclusions can be reached by statistical study. A study by Miss Lane-Claypon[6] is based on data collected from records of twelve leading hospitals of Great Britain, in which the frequency of cancer of the breast which occurred in parous and nulliparous women

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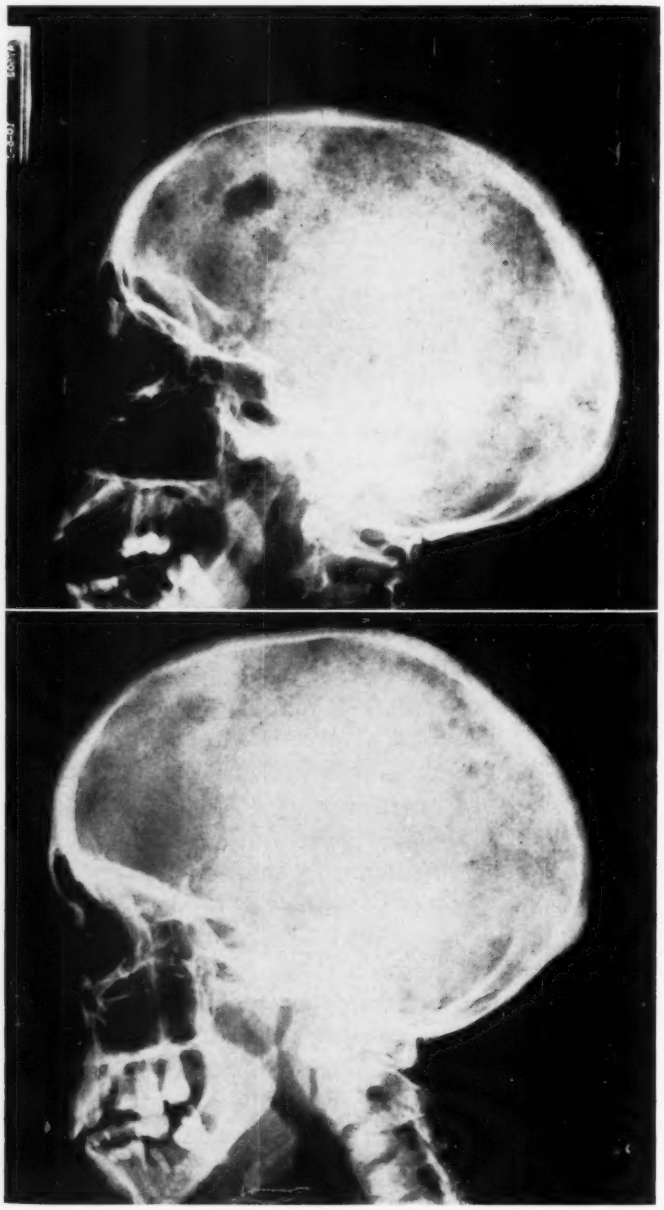
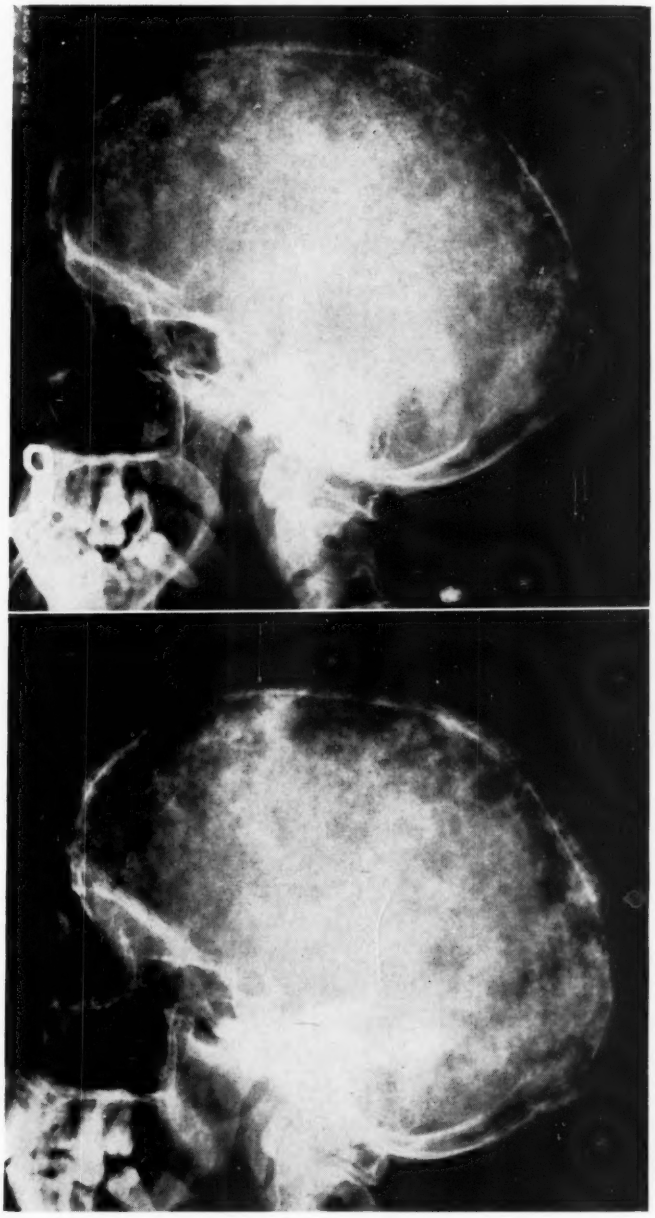


B.

Fig. 1, *A* and *B*.—*A*, X-ray of skull made on admission of pregnant woman; *B*, x-ray of skull made just prior to radical mastectomy.

in all hospital admissions and considered in specific age groups. From this study there was a definitely greater frequency in women never pregnant. In another statistical study Peller[7] found breast cancer equally frequent in women never pregnant and those having been pregnant. Oddly, however, he found that in considering only women having borne children that the frequency of breast

C.



D.

Fig. 1, *C* and *D*.—*C*, X-ray of skull made four months after radical mastectomy; *D*, x-ray of skull made just prior to death (S.P. 9357). (See Table III.)

cancer was in inverse proportion to the number of children born, that is, breast cancer occurred more often in women having one pregnancy than women having borne several children.

Trout[8] has recommended advising against pregnancy because of the danger of a new cancer arising in the remaining breast after radical mastectomy for cancer. Kilgore[4, 5] recommended a prophylactic early removal of the other breast if no axillary metastases were found in the specimen removed by radical mastectomy and also in instances with axillary metastases and showing no evidence of recurrence at the end of three years because, as he says, a woman is three to four times more likely to have cancer in the one breast remaining after radical removal of the other for cancer than is a woman with two normal breasts. We are inclined to believe that there is something to be said for the inclusion of the other breast in the bloc removed if the primary tumor is in the medial hemisphere. Recently we have suggested the desirability of removing the other breast for a reason which, as far as we know, has not been mentioned by anyone; that is, for a cosmetic result. Although this suggestion has, except in one instance, not been accepted, several patients have stated later that they regretted not having done so. This, of course, is particularly true in instances of large pendulous breasts in which radical mastectomy produces such marked asymmetry.

The appearance of cancer in the other breast, simultaneously or after a radical mastectomy, always leaves one in doubt whether it is a metastasis or a new tumor. If one accepts the idea of cancer of the breast extending itself by invasion in continuity in all directions rather than by embolism (which theory is after all the sole basis of a surgeon's employment of the principle of a wide one-piece bloc removal), "the other breast" is quite as much in the field of regional recurrence as is the axilla of the breast which was the site of origin of a cancer. It is easy to understand why the stimulation to more rapid growth of a nidus of the original tumor which had extended to the other breast would appear as a repetition of the previous catastrophe. Also there is no evidence contrary to the conclusion that the other breast is not subject to the same frequency of origin of cancer as is a designated breast of a normal woman of the same age.

In both patients reported by Trout[8] pregnancy and the appearance of cancer in the other breast were within the period in which a recurrence of the original tumor could have been expected. In Warren and Gates'[9] extensive study of multiple malignant tumors in one individual, they found records of only 47 instances in which there was evidence worth considering of independent origins of cancer in both breasts. In only 4 of these was the interval between the discovery of the 2 tumors in excess of four years. In 6 instances the tumors appeared simultaneously. In the remainder, the interval was not stated or was less than four years.

This study we believe justifies the following statements:

1. We can find no evidence to support the idea that pregnancy can ever be considered as an influential agent in originating a cancer of the mammary gland. In reality there is at least some evidence to the contrary.

2. It would appear that there could be no reasonable doubt that pregnancy exerted a strong influence on a coexisting cancer of the breast to increase the rapidity of its growth and rate of its extension from the site of origin. The mechanism of this influence would appear to be the same as that which causes the well-known anatomic changes in the normal mammary gland during pregnancy. This mechanism is by no means clear, but one cannot escape the conclusion that the primary stimulus for setting it in motion must arise in the fetus and not in the mother.

3. The indications for the removal of the other presumably normal breast simultaneous with or subsequent to a radical operation for cancer of the breast should be based on the assumption that cancer may have already extended to the normal breast or, in other words, for the same reason that the contents of the axilla should be included in the bloc removed. This statement is of particular importance in instances in which a cancer arises in the medial hemisphere of the mammary gland, in some of which the primary neoplasm is nearer the other breast than to the axilla of the one diseased.

4. Whether or not a patient during the childbearing age, operated upon for cancer of the breast, is to be advised against pregnancy, told it is not contraindicated, or a discussion of the subject entirely omitted is solely an affair of the surgeon and the patient and each instance should have individual consideration based entirely on the surgeon's judgment as to the probability of the complete removal of all the neoplasm and the patient's ability to understand and choose the amount of risk involved for diminishing an already short life expectancy if all the tumor is not removed. With residual cancer the life expectancy, already short, would be further shortened by pregnancy, but one can well imagine that the sum total of happiness of a childless woman living for an additional four years might be less than her living for only one year if this one year were composed of nine months of anticipation and three months was realization of having accomplished her most primitive obligation for the survival of the race. It is worth while pointing out that of the 11 patients reported in this paper in which pregnancy and cancer of the breast were associated, 10 of them have produced normal children and the other 1 will presumably do so shortly.

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STUDIES IN VIRULENCE OF CLOSTRIDIUM WELCHII

W. A. Altemeier, M.D., and W. L. Furste, M.D., Cincinnati, Ohio

(From the Department of Surgery of the University of Cincinnati College of Medicine and Cincinnati General Hospital)

ALTHOUGH the spectacular nature of gas gangrene as a complication of wounds of violence has always excited considerable interest, relatively little has been learned regarding the factors which precipitate this infection. Its characteristic pathologic appearance has established the disease as a clinical entity, and numerous bacteriologic studies have confirmed its multiple bacterial etiology. A great variety of gas-producing, anaerobic bacteria have been repeatedly found in association with this condition, but the fact remains that the *Clostridium welchii* is the principal cause of gas gangrene and is present either alone or in association with other gas-producing anaerobes in 56 to 100 per cent of the cases studied (Table I).

Since World War I, it has been established that *Cl. welchii* is practically ubiquitous in the human environment. It has been repeatedly isolated from many sources including the soil, intestinal canals of man and animals, sewage, hair of domestic animals, dust samples taken from a variety of sources including a warship and the floors of homes or public buildings, vaginal tract, skin of the human abdominal wall, and even milk, fish, cheese and ice.[4, 9-15] Because of its widespread distribution, its contamination of a considerable proportion of open wounds of violence is almost inevitable. This is particularly true of severe injuries which have been soiled by dirt, clothing, cinders, or splinters. Recent studies have shown the presence of *Cl. welchii* as a primary contaminant in 3.8 to 39.4 per cent of the wounds investigated, the average incidence of contamination in 3,027 collected wounds being 14.7 per cent.

In contrast to the high incidence of contamination of wounds by *Cl. welchii*, the development of clinical gas gangrene is relatively infrequent (Table III). Its incidence has varied between 0.2 per cent and 5.26 per cent. In a collected series of 187,636 major open wounds, the average incidence of gas gangrene as an infectious complication was 1.62 per cent.

A review of the known predisposing and exciting etiologic factors fails to explain the low incidence of gas gangrene in the face of the high incidence of *Cl. welchii* contamination. This infection has always been a disease associated with violence and has been most likely to develop in wounds containing crushed or torn muscle and dirt, such as extensive lacerations, compound fractures, fracture dislocations, or crushing injuries. An experimental study was therefore undertaken to measure accurately the effect of crushed muscle and dirt on the pathogenicity of a strain of *Cl. welchii* of maintained virulence and to determine the importance of these two factors in the development of gas gangrene.

MATERIAL

Guinea pigs weighing 350 to 450 grams were chosen as the experimental animals because their marked susceptibility to *Cl. welchii* infection resembled

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that of the human being. The virulence of many strains of *Cl. welchii* which were obtained from a variety of sources including soil, clothing, and contaminated or infected wounds was investigated by determining the minimum lethal dose and toxigenicity for these animals. For most of the strains tested, the virulence and toxin production were either relatively low or very variable. A satisfactory strain of high virulence known as BP6K was obtained.*

TABLE I. THE REPORTED FREQUENCY OF CL. WELCHII IN ESTABLISHED GAS GANGRENE

	PERCENTAGE INCIDENCE OF CL. WELCHII IN GAS GANGRENE
Babcock[1]	72
Bates[2]	About 80
Boyd[3]	70-80
Cruickshank[4]	70-80
Gins and Koeppen[5]	96
MacLennan[6]	56
Weinberg and Seguin[7]	85
Kukin[8]	100

TABLE II. THE INCIDENCE OF CL. WELCHII CONTAMINATION IN WOUNDS OF VIOLENCE

	NO. OF CASES	NUMBER CONTAMINATED WITH CL. WELCHII	PERCENTAGE OF CASES CONTAMINATED WITH CL. WELCHII
Altemeier and Gibbs[16]	99	39	39.4
DeWaal[17]	708	27	3.8
Dimtza and Gutscher[18]	424	57	13.4
Meleney[19]			
Soft part wounds	926	138	14.9
Compound fractures	674	147	21.8
Levaditi et al[20]	61	10	17.0
Miles[21]			
Military wounds	105	24	22.8
Spooner[22]	30	3	10.0
Total	3027	445	14.7

TABLE III. THE REPORTED INCIDENCE OF GAS GANGRENE IN WOUNDS OF VIOLENCE

	NO. OF CASES	NUMBER OF CASES WHICH DEVELOPED GAS GANGRENE	PERCENTAGE OF CASES WHICH DEVELOPED GAS GANGRENE
Altemeier[23]	71	3	4.2
Callender and Coupal[24]			
Soft part wounds	128,265	1389	1.08
Wounds including bone fracture	25,272	1329	5.26
DeWaal[17]	708	3	0.42
Fisher, Florey, Grimson, and Williams[25]	3,471	5	0.15
Jeffrey[26]	About 2,000	5	0.25
Langley and Winkelstein[27]	6,000	96	1.6
Lenner[28]	750	18	2.4
MacLennan[29]	About 6,800	44	0.6 to 0.7
Neel and Cole[30]		(British Campaign in Tripolitania & Tunisia)	
Cases in Pacific area	984	7	0.71
Power[31]	6,000	20	0.3
Ross and Ryan[32]	1,815	82	4.5
Tuchel and Cureumeli[33]	2,500	20	0.8
Wan[15]	3,000	17	0.6
Total	187,636	3008	1.62

*From Dr. Milan Logan of the Department of Biochemistry.

When cultured in pancreatic digest medium developed by Dr. Logan, the virulence of this strain was much greater than when grown in deep meat broth, brain broth, or other media. Cultures incubated for 4½ to 6 hours produced death in much higher dilutions than those incubated for 18 to 24 hours. Also, it was learned that weekly passage through pigeons was necessary to maintain its virulence at a high level. Serial dilutions of a 4½ to 6 hour culture were made to the tenth power using pancreatic digest medium for the diluent.

METHOD

Three methods of determining the virulence of clostridia have been used in previous experimental work:

1. The injection of measured amounts of a culture or its dilution intramuscularly through a fine gauged needle.
2. The injection of measured amounts of a culture or its dilution in the presence of some locally irritating substance such as calcium chloride.
3. The injection of measured amounts of a culture or its dilution into wounds containing devitalized muscle produced by mechanical means.

Experimental infections produced by the last procedure seemed to simulate more closely the type of gas gangrene which develops clinically. The following method was used to compare the virulence of *Cl. welchii* in healthy viable muscle with that in the presence of traumatized muscle with and without contamination by sterilized dirt.

On different days, two experiments were done, each consisting of three groups of twenty to twenty-five animals. In the first group, the skin over the lower back and posterolateral aspects of the thigh was prepared by shaving and scrubbing with soap and water for ten minutes while the guinea pigs were fastened in the prone position. The preparation was completed by the application of alcohol, ether, and tincture of iodine. These steps were taken to eliminate or minimize the introduction of *Cl. welchii* spores normally resident on the skin or hair of the guinea pig. By means of a fine tuberculous syringe and a 25 gauge needle, 0.5 c.c. of the various serial dilutions of a 4½ to 6 hour culture of *Cl. welchii* was injected through the skin into healthy muscle, five animals being used for each dilution.

In the second group, after the induction of drop ether anesthesia, an incision 1.0 cm. in length was made under aseptic technique through the similarly prepared skin and subcutaneous tissues of the thigh and developed down to and beyond the femur. The muscles on each side of the wound were crushed five times with a Kocher clamp, and then lacerated by twisting the clamp. The edges of the wound were closed with interrupted fine black silk sutures to prevent or minimize leakage of the inoculum and secondary contamination. Injections of the serial dilutions of a culture of *Cl. welchii* were then made into the area of traumatized muscle through a 25 gauge needle introduced about 0.5 cm. from the wound margins, five animals being used for each dilution.

In the third group, wounds were prepared in exactly the same manner as in the second group with the exception that 1.0 c.c. of an autoclaved and finely divided mixture of soil and cinders was placed into the wound just before its

closure with interrupted sutures of fine black silk. Injections of the various serial dilutions were then made into the areas of crushed muscle and dirt, five animals being used for each dilution. In this way, different and measured amounts of virulent bacteria were injected into healthy muscle in one group, into areas of devitalized muscle in the second, and into areas of devitalized muscle contaminated by sterile dirt in the third. Subsequently, the characteristics and size of the wounds which developed were noted and the date of death determined in each instance. In this manner the minimum lethal dose of *Cl. welchii* was determined in the three groups and it was considered to be 0.5 c.c. of the highest dilution which killed all the guinea pigs in 4⅔ days under the conditions of the experiment.

Fig. 1.—Example of a guinea pig which survived an injection of 0.5 c.c. of 10^{-3} dilution (.1 MLD) of a five-hour culture of *Cl. welchii* strain BP6K when the inoculation was made into healthy normal muscle fifteen days previously. The original gangrenous lesion is undergoing spontaneous healing.

RESULTS

When serial dilutions of *Cl. welchii* were injected into areas of healthy muscle (Fig. 1), the minimum lethal dose was found to be 0.5 c.c. of a 10^{-2} dilution. When serial dilutions were injected into wounds containing crushed devitalized muscle (Fig 2), the minimum lethal dose was found to be 0.5 c.c. of a 10^{-5} dilution. Thus, it took 1,000 times less bacteria to produce consistently a fatal gas gangrene in the presence of devitalized muscle than it did when injections were made into healthy muscle. In the third group in which serial dilutions were injected into wounds containing both devitalized muscle and pulverized dirt, the minimum lethal dose was 0.5 c.c. of 10^{-8} dilution (Fig. 3).

Thus, in two experiments done on different days, it took one million times less bacteria to produce a fatal gas gangrene in guinea pigs in the presence of devitalized muscle and dirt than it did when injections were made directly into healthy muscle (Table IV).

The lesions of gas gangrene which developed in the animals injected with a lethal dose of *Cl. welchii* were very extensive and severe, and the following external changes took place (Fig. 2). Within twelve hours a reddish brown and crepitant area of swelling measuring several centimeters in diameter usually had developed. The area of edema rapidly increased in the next two or three days,

Fig. 2.—Illustrating the enhancing effect of crushed muscle on the virulence of *Cl. welchii*. An extension and fatal infection has been produced by only 0.5 c.c. of a 10^{-3} dilution of the same culture when injected three days previously into a closed wound containing crushed muscle.

usually spreading on to the abdominal and thoracic walls, and became green and subsequently gray or black. If the animal survived a period of more than three days, the area of gangrene sloughed and discharged a thin, black liquid containing bubbles of gas and having a foul odor. Death occurred within one to four days, depending upon the size of the dose and the individual resistance of the animal.

When determinations of the minimum lethal dose in the presence of crushed muscle and dirt were made in fifteen other groups consisting of fifteen to twenty-five animals over a period of five months, unexplained variations of the minimum lethal dose occurred between 0.5 c.c. of 10^{-6} and 10^{-10} dilutions of 4½ to 6 hour

culture of *Cl. welchii*. The average minimum lethal dose, however, was 0.5 c.c. of a 10^{-8} dilution.

DISCUSSION

It has long been recognized that certain types of wounds such as extensive lacerations, compound fractures, or crushing injuries are particularly prone to develop gas gangrene. Larrey,[34] Surgeon-in-Chief of the French Armies under Napoleon, believed that it was advisable to amputate badly traumatized limbs within the first twenty-four hours, thereby converting them into wounds capable of being speedily healed and obviating the causes of gangrene. He cited the high incidence of fatal gangrene and tetanus in the experiences of other contemporary surgeons who temporized for several or more days before amputating the stumps of limbs shot away.

Fig. 3.—Further enhancement of the virulence of *Cl. welchii* by contamination of traumatized muscle with sterile dirt as evidenced by a fatal infection following the injection of 0.5 c.c. of a 10^{-8} dilution of the same culture.

Although some of the factors responsible for the development of gas gangrene are still unknown, these experimental studies emphasize quantitatively the role played by devitalized muscle and dirt in its pathogenesis. It is not clear what determines the potential virulence of the *Cl. welchii* contaminating a wound, and our studies indicate that the virulence of the same strain may vary considerably over a five-month period even under apparently identical condi-

TABLE IV. COMPARING THE EFFECT OF CRUSHED MUSCLE AND DIRT ON THE VIRULENCE OF CL. WELCHII

CONDITIONS OF EXPERIMENT	TOTAL NO. OF GUINEA PIGS	NO. OF ANIMALS FOR EACH DILUTION	MLD 0.5 C.C. OF FOLLOWING DILUTION
Injection of culture only	45	10	10^{-2}
Injection of culture in presence of crushed muscle	50	10	10^{-5}
Injection of culture in presence of crushed muscle and dirt	50	10	10^{-8}

tions. However, it becomes obvious that if a virulent strain finds its way into a wound containing devitalized muscle and dirt, the chances for the development of infection are tremendously enhanced.

Devitalization of muscle and other tissues may be caused directly by trauma or indirectly by impairment of the blood supply. It is an established fact that the incidence of gas gangrene is five to six times higher in compound fractures than in soft tissue wounds. Callender and Coupal[24] found that the incidence of gas gangrene was 5.26 per cent in 25,272 compound fractures in the American Expeditionary Force and only 1.08 per cent in 128,265 soft tissue wounds. Thrombosis, ligation, or spasm of large arteries may result in the necrosis of tissue. Muscles or parts of muscles may become ischemic if their nutrient arteries are injured, and re-establishment of collateral circulation appears to be extremely slow. When a muscle is deprived of its blood supply for six or eight hours, it usually dies. Trueta[35] and MacLennan[29] both emphasized the importance of an inadequate blood supply in the pathogenesis of gas gangrene.

Improper surgical care also may be responsible for the formation of devitalized tissue within a wound. The prolonged application of a tourniquet, a delay in initial surgical care, inadequate débridement, packing of wounds tightly, closure of wounds under tension, closure of incompletely débrided military or civilian wounds, and the application of improperly fitting or constricting bandages, casts, or splints, all favor the development of devitalized tissue and gas gangrene. Closure of incompletely débrided war or civilian wounds is particularly dangerous.

SUMMARY AND CONCLUSIONS

Although wounds of violence have been commonly found to be contaminated with *Cl. welchii,* only 0.2 to 5.26 per cent of them have developed gas gangrene. A review of the known predisposing and exciting etiologic factors has failed to explain the low incidence of infection. The effect on the pathogenesis of gas gangrene by two factors, devitalized muscle and dirt, commonly associated with the disease clinically, has been carefully measured in two controlled experiments using 145 guinea pigs. It took one thousand times less *Cl. welchii* to produce a fatal gas gangrene when the bacteria were injected into devitalized muscle than it did when they were injected into healthy muscle. Furthermore, one million times less organisms were necessary to cause a fatal infection when the bacterial injections were made into areas of devitalized muscle contaminated with sterile dirt.

Some of the factors precipitating this infection are still unknown, but these results clearly illustrate the effect that devitalized muscle and dirt have in en-

hancing the virulence of *Cl. welchii* in wounds of violence, thereby favoring the development of gas gangrene.

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FURTHER EXPERIMENTS WITH NONIRRITATING GLOVE POWDER

E. Meredith Alrich, M.D., Charlottesville, Va., C. Marshall Lee, Jr., M.D., Asheville, N. C., and Edwin P. Lehman, M.D., Charlottesville, Va.

RECENTLY Lee and Lehman[1] reported the effects of talcum powder and other agents proposed as replacements for talcum powder, in the peritoneal cavity. These studies clearly indicated the danger of talc as an adhesion-producing agent. One of the other agents which was a starch product* designated as No. 108 was found to be particularly adaptable in its physical properties to replace talcum powder and did not cause adhesion formation in the peritoneal cavity. This product, which is a soluble starch, was made only in small amounts and under experimental conditions. The manufacturers have recently put this powder into mass production for commercial use. We felt that similar experimental investigation of the effects of this commercially prepared product should be carried out to determine if it was identical in all respects with the original experimental product.

The two products tested will be designated as 108 and Batch No. 2, 108. Both of these powders were found to have identical physical properties and were equally satisfactory as a glove powder; autoclaving did not effect their flow and dusting qualities. The method of testing intraperitoneal reaction to the powders was identical with that in the previous report. Dogs were used, the abdomen being opened through a standard right rectus incision. Rigid, aseptic technique was employed throughout, except that before beginning the operation both operator and assistant washed their gloves thoroughly under running tap water. One-half teaspoonful of the test powder was then lightly dusted over the entire bowel and mesentery surfaces as evenly as possible and the wound closed in layers with silk. The animals were reoperated upon after an interval of four to five weeks and the presence of adhesions carefully recorded by counting by the method of Lehman and Boys.[2] Each of the two powders was tested in a series of twenty animals.

Table I. Further Experiments With Nonirritating Glove Powder

TYPE OF POWDER	AMOUNT OF POWDER	EQUIVALENT IN GLOVE WASHINGS	NUMBER OF DOGS	AVERAGE NUMBER OF ADHESIONS	GREATEST NUMBER OF ADHESIONS	SMALLEST NUMBER OF ADHESIONS
Starch 108	½ tsp.	8 pairs	20	0.2	1	0
Starch 108 reprocessed	½ tsp.	8 pairs	20	0.9	6	0
Talcum powder[1]	½ tsp.	8 pairs	10	XXXX	XXXX	XXXX

XXXX, adhesions too numerous to count.

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*Made available to us by the Department of Clinical Research, Ethicon Suture Laboratories, Division of Johnson & Johnson, New Brunswick, N. Y.; now marketed as Biosorb.

RESULTS

The results are recorded in Table I. There is included a control series of ten animals copied from Lee and Lehman[1] in which a similar amount of talcum powder was used. The 108 and Batch 2, 108 powders produced insignificant adhesion formation as compared with the animals in which talcum powder was used, there being no essential difference in the two starch products.

CONCLUSION

Commercially prepared powder, Batch 2, 108, is a safe and satisfactory glove powder.

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COMPARISON OF TISSUE REACTION TO TALC AND MODIFIED STARCH GLOVE POWDER

R. W. Postlethwait, M.D.,* H. Lee Howard, M.D.,
and Paul W. Schanher, M.D., Durham, N. C.

(From the Departments of Surgery and Pathology, Duke University School of Medicine, Duke Hospital)

TALC, used as a surgical glove lubricant, is frequently implanted in the wound during operation. The granulomatous reaction produced by the talc may result in dangerous complications. In the abdomen, dense adhesions may lead to intestinal obstruction. The foreign body response of the tissues attempting to extrude talc crystals may be manifested by a persistent draining sinus. The foreign body reaction to encapsulate the talc may form a nodule or nodules in the wound. Complications may be minor and merely annoying, as a small nodule in the wound, but in occasional patients subsequent major operations may be necessary, at times resulting in death.[2]

The sources of implantation of a surgical glove lubricant into the wound are readily recognized: (1) From a tear or perforation of a glove (Weed and Groves[9] found perforations present in 22.5 per cent of 35,763 gloves used in 4,549 operations. At this hospital, it has been found in a smaller series that 16.7 per cent of 8,893 gloves used in operations were perforated. Seelig[8] stated that 50 to 100 mg. of powder may be present in the finger tip of a glove). (2) From unwashed gloves. Even if thoroughly washed, a thin film of powder remains on the gloves. (3) As spill from gloves or powder containers (either envelopes or shakers) onto instruments, sponges, and suture material. (4) From air-borne transmission when applying glove lubricant to the hands. (5) From rising particles of powder if a sponge is thrown into the bucket containing the discarded excess powder.

The exact amount of talc necessary to produce a pathologic response in human beings is unknown. The location of the talc adhesions and granuloma would seem more important, as a minute reaction strategically located might produce adhesions resulting in intestinal obstruction. In addition, individual variation in reaction to talc may be a factor of considerable consequence.

The frequency with which talc granulomas are found depends upon the thoroughness of the search for such lesions. At this hospital, six patients with complications due to talc granulomas were seen in a short period of time after polarized light was used to examine suspicious tissues. Two patients had small nodules develop in the scar following radical mastectomy. Excision resulted in correct diagnosis of talc granuloma but the possibility of a recurrence of the neoplasm caused concern. Talc was found in intra-abdominal adhesions of two patients; one had undergone two, and the other five previous laparotomies. One

Aided by a grant from Ethicon Suture Laboratories, Division of Johnson & Johnson, New Brunswick, N. J., who also furnished the starch powder.

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*Now at Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N. C.

patient had an appendectomy followed by the development of a 6 by 10 cm. right lower quadrant mass several weeks later. Exploratory laparotomy and later a biopsy of the abdominal wall mass, due to talc, was followed by an incisional hernia which subsequently required repair. The last patient had several nodules in the abdominal scar after combined abdominoperineal resection.

In the fifteen years since Antopol[1] first directed attention to these lesions, surgeons have become increasingly aware of the need for a satisfactory substitute for talc. The work toward this objective is well summarized in the papers of Seelig and his co-workers,[2, 6, 7, 8] of Lee and Lehman,[3] of Lichtman, McDonald, Dixon, and Mann,[4] and of MacQuiddy and Tollman.[5]

The most promising of the various materials suggested as substitutes for talc is a starch powder first reported by Lee and Lehman. This starch, called by them powder No. 108, is "a mixture of amylose and amylopectins derived from cornstarch and containing a small amount of magnesium oxide, which has been treated by physical and chemical means to improve its lubricating value and to prevent gelatinization when autoclaved." It has been commercially named Bio-sorb. Lee and Lehman confirmed that an extensive granulomatous reaction with adhesion formation followed the implantation of talc into the peritoneal cavities of dogs. The starch powder similarly applied to the peritoneal cavity was absorbed without reaction. MacQuiddy and Tollman attempted in patients and in animals to produce evidence of sensitivity to the same starch powder, but failed to demonstrate any allergenic properties.

As it is obvious that a definite and immediate need to replace talc as a surgical glove lubricant exists, the following studies, partially confirmatory, were carried out. The starch was the same powder, No. 108, used by Lee and Lehman, and by MacQuiddy and Tollman. Briefly, gross and microscopic tissue reaction to starch and talc was observed in animals in which the material had been placed in the peritoneal, pleural, and pericardial cavities, and within muscle, tendon, joint, and nerve.

METHODS

The majority of the dogs had been used by students during their instruction in surgical technique. All procedures were carried out under rigidly aseptic conditions. Each dog had undergone cholecystectomy, cecectomy, and either enteroenterostomy or gastroenterostomy at two-week intervals. Thirty-two such animals were autopsied and no peritoneal reaction could be demonstrated except a few adhesions at the operative sites in some dogs. In every animal, the peritoneum in the left lower quadrant was entirely normal. In the next twenty-four dogs at the last operation 1 Gm. of starch or talc was carefully spread over the bowel in the left lower quadrant without trauma to the peritoneal surfaces. These animals were autopsied between fourteen and twenty-eight days.

In fifteen dogs under endotracheal ether anesthesia 1 Gm. of starch or talc was placed in each pleural cavity, and 0.1 Gm. in the pericardial sac. Particular care was used to wash thoroughly the gloves worn during the operative procedure. In six dogs, short longitudinal incisions were made to each side of the midline just below the costal margin, the anterior rectus sheath opened, and approximately the anterior two-thirds of the rectus muscle cut transversely. A small pinch of material, talc on one side and starch on the other, was then

placed in the muscle and the skin closed. Both Achilles' tendons were cut halfway across and the test material placed over the cut ends. One fine black silk suture reapproximated the tendon and the skin was closed. In three dogs, the sciatic nerves were exposed, cut in half, the material applied, and the ends approximated with one silk suture. In another group of six dogs a median parapatellar incision was made bilaterally, the knee joints entered, and a pinch of the material placed in the joint. Closure was performed with silk. All dogs were sacrificed in fourteen to twenty-eight days.

Four dogs and nine rabbits had 1 Gm. starch placed in the peritoneal cavity. The animals were reopened at intervals from two hours to thirty-seven days to determine absorption time of the starch.

RESULTS

Peritoneum.—Talc: Grossly, all twelve animals showed a massive reaction with broad bands of connective tissue and yellow granulomatous nodules, matting together of loops of small bowel and omentum with adherence to the abdominal wall. *Microscopically,* the reaction was granulomatous without pseudotubercle formation, but with the macrophage predominating throughout a background of fibroblasts, collagen, and proliferating capillaries (Fig. 1). A small number of round cells and plasma cells were seen and only a rare polymorphonuclear leucocyte was present. These masses were covered by peritoneum. Under ordinary light, slightly bluish crystals of varying sizes and shapes were seen in the macrophages. Many of the phagocytic cells were forming giant cells of the foreign body type about the larger crystals. Studies under polarized light showed the crystals to be doubly refractile (Fig. 2). A water suspension of talc showed anistropic crystals of various sizes and shapes. *Starch:* Grossly, none of the dogs showed adhesions, but two of the twelve showed a few firmly adherent, small 1 to 2 mm. whitish-yellow nodules over portions of the small bowel and spleen. Microscopically, the ten grossly negative animals showed only slight swelling of the peritoneal lining cells (Fig. 1). Sections of the small whitish-yellow nodules revealed them to be granulomas similar to those produced by talc, but containing fewer fibroblasts, less collagen, and more small round cells, as well as polymorphonuclear leucocytes. Throughout these small granulomas, oval bodies (15-30 micra in diameter) could be seen. These bodies, which had a cross configuration in the center, were adjacent to large mononuclear cells, but rarely engulfed by them. With polarized light, these bodies were doubly refractile with a distinctive black Maltese cross configuration in the center (Fig. 2). A water suspension of the starch powder showed numerous identical refractile oval bodies, with a black Maltese cross pattern in the center.

Pedicardium.—Talc: Grossly, all eight animals were found to have fibrous and fibrinous adhesions, as well as small yellow nodules. Microscopically, the typical talc reaction was found, but in three animals it was less marked than in the others. *Starch:* Grossly, six of the seven dogs showed no reaction. One dog was found to have delicate adhesions, but no visible yellow nodules. Microscopically, the six grossly negative animals showed only swelling of the lining cells. The one animal was found to have a granulomatous reaction with visible starch crystals.

Pleura.—Talc: Grossly, in all fifteen, adhesions and yellow granulomatous nodules were found. Two, however, were not extensive. Microscopically, the typical talc reaction was found, but in three animals it was less marked (Fig. 1). *Starch:* Grossly, twelve of the fifteen pleural cavities were negative. Two contained several focal adhesions, and one had massive adhesions and many granulomatous nodules. Microscopically, ten dogs showed no reaction (Fig. 1). Four had small starch granulomas, and one had an extensive granulomatous process with marked fibroblastic proliferation. In the latter animal, however, the crytsals had the configuration of talc rather than starch. (It is believed that a spill of talc occurred from the pericardium.)

Tendon.—Talc: Grossly, all six tendons showed swelling and hyperemia. Microscopically, talc granulomas were found in all. *Starch:* Grossly, swelling and hyperemia were seen in all six animals. Microscopically, two showed no reaction, but minimal starch granulomas were seen in three. An extensive reaction with only a few starch crystals was found in one.

Knee Joint.—Talc: Grossly, no gross lesions were noted in the six dogs. Microscopically, five showed small talc granulomas with early villous formation, and one revealed no reaction. *Starch:* Grossly, no gross changes were seen. Microscopically, all exhibited tissue reaction, but only rarely were starch crystals seen.

Nerve.—Talc: Grossly, all three revealed swelling and induration. Microscopically, all three demonstrated talc granulomas; one, however, was minimal. *Starch:* Grossly, two showed swelling and induration and one was negative. Microscopically, all exhibited tissue reaction, but only rarely were starch crystals seen.

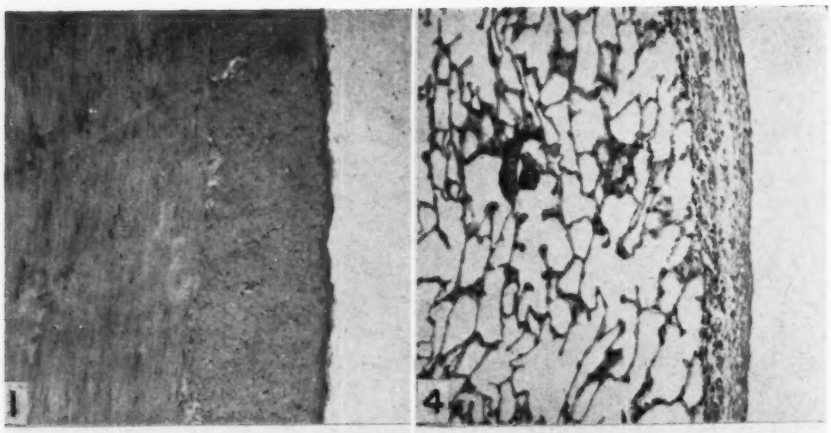
TABLE I. RESULTS OF TALC AND STARCH IMPLANTATION IN PERITONEUM, PERICARDIUM, AND PLEURA

	NO. OF DOGS AND MATERIAL USED		NO REACTION		SLIGHT REACTION		MARKED REACTION	
			GROSS	MICRO.	GROSS	MICRO.	GROSS	MICRO.
	32	None	32	5*	0	0	0	0
Peritoneum	12	Talc	0	0	0	0	12	12
	12	Starch	10	10	2	2	0	0
Pericardium	8	Talc	0	0	0	0	8	8
	7	Starch	6	6	1	1	0	0
Pleura	15	Talc	0	0	2	3	13	12
	15	Starch	12	10	2	4	1†	1†

*Sections made on only five.
†Talc crystals present, undoubtedly from pericardium.

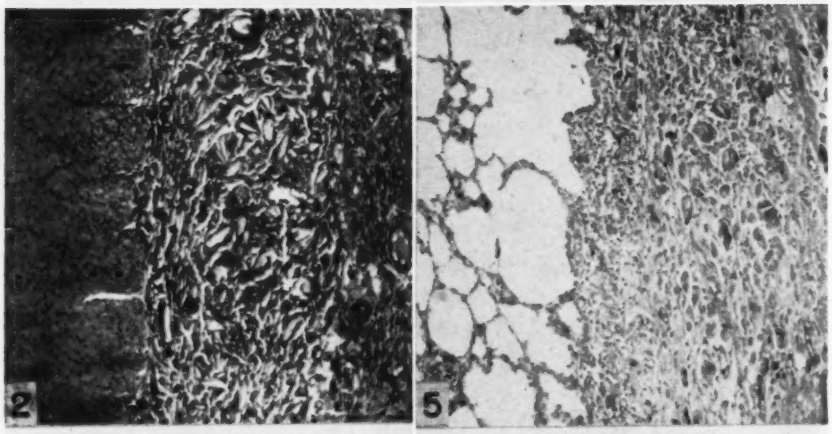
TABLE II. RESULTS OF TALC AND STARCH IMPLANTATION IN TENDON, JOINT, MUSCLE, AND NERVE

ANIMAL NO.		1		2		3		4		5		6	
		GROSS	MICRO.	GROSS	MICRO.	GROSS	MICRO.	GROSS	MICRO.	GROSS	MICRO.	GROSS	MICRO.
Tendon	Talc	++	++	++	+++	+	++	+	++	+	+++	++	+
	Starch	++	0	+	+	++	++	++	0	+	+	+	+
Joint	Talc	0	+	0	0	0	+	0	+	0	++	0	++
	Starch	0	0	0	0	0	0	0	0	0	0	0	0
Muscle	Talc	0	+++	+	+++	+	++++	0	+++	0	+++	+	++++
	Starch	0	0	0	0	0	0	0	+	0	0	0	0
Nerve	Talc	+	+	+	++	+	++						
	Starch	+	+	0	+	+	+						



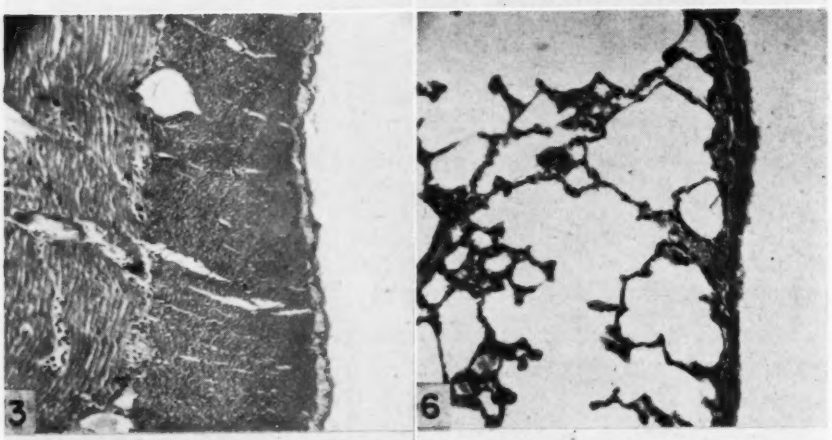
PERITONEUM
Control
Dog

PLEURA
Control
Dog



PERITONEUM
Talc
Dog

PLEURA
Talc
Dog



PERITONEUM
Starch
Dog

PLEURA
Starch
Dog

Fig. 1.

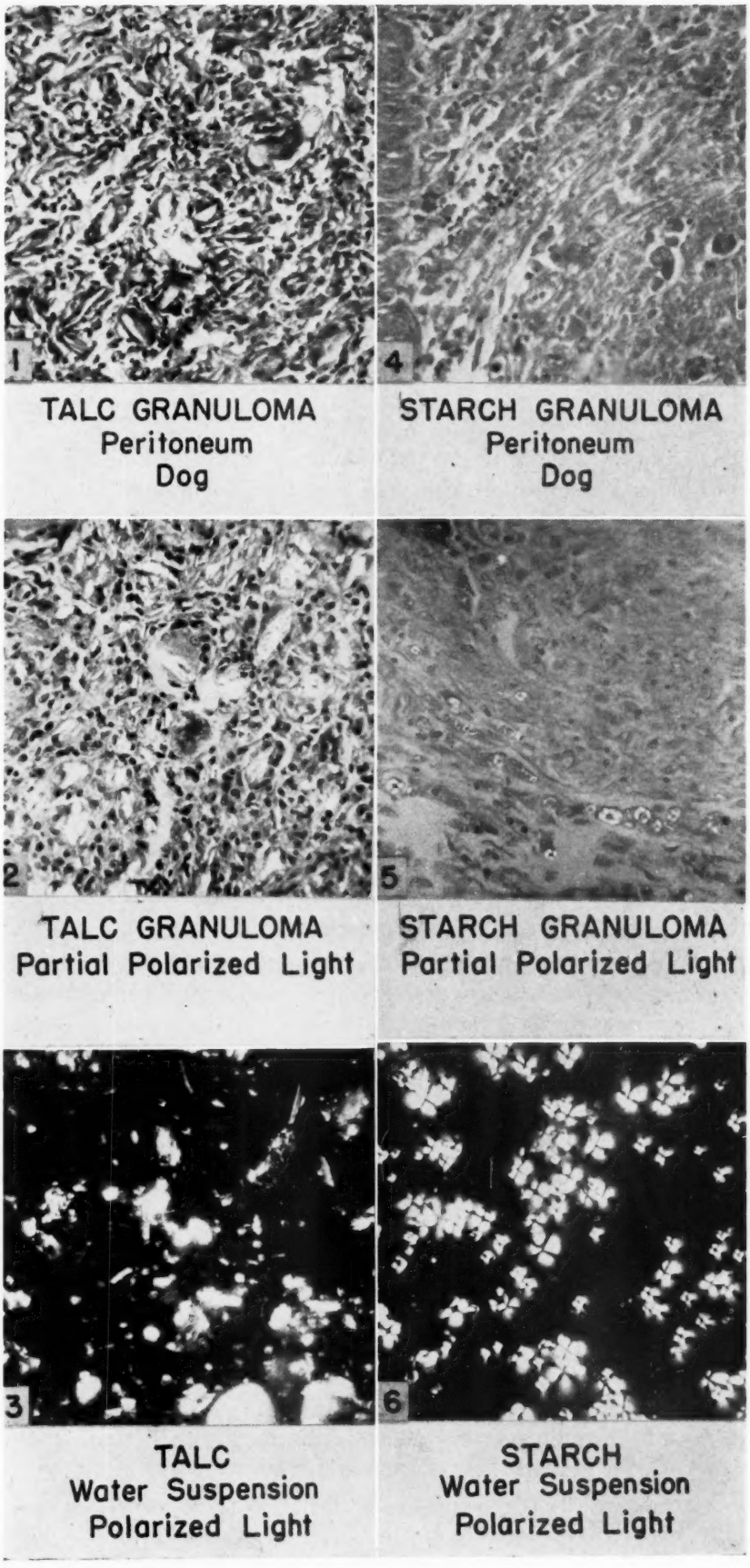

1
TALC GRANULOMA
Peritoneum
Dog
4
STARCH GRANULOMA
Peritoneum
Dog
2
TALC GRANULOMA
Partial Polarized Light
5
STARCH GRANULOMA
Partial Polarized Light
3
TALC
Water Suspension
Polarized Light
6
STARCH
Water Suspension
Polarized Light

Fig. 2.

Muscle.—Talc: Grossly, three showed yellow nodular areas in the muscle; three were negative. Microscopically, extensive talc granulomas were present in all six. *Starch:* Grossly, all six dogs were negative. Microscopically, five animals showed no reaction, and one had a minimal starch granuloma.

Absorption Experiments.—After intraperitoneal implantation of 1 Gm. of starch the incision was reopened in one rabbit for each period at the end of 2, 4, 8, 12, 24, and 48 hours, and 7, 11, and 16 days. Each rabbit showed smooth oblong masses of starch up to 0.5 cm. in length, loosely attached to the peritoneum or free in the right lower quadrant. A few showed excess clear, yellow fluid, and after 24 hours, delicate adhesions appeared. At the end of 10 days, another gram of starch was placed in the left lower quadrant in 7 of the 9 rabbits. These were then reopened at the following intervals after the second starch implantation: 17, 18, 19, 20, 33, and 37 days. In 2 of the rabbits, opened in 18 and 33 days, no plaques of starch were found, although moderately firm adhesions were present. In the remaining rabbits, plaques of starch as just described were noted. In the rabbits opened at the longer intervals, the adhesions were found to be firmer, but not extensive. No essential differences were found in the two lower quadrants, except that starch plaques were sometimes present in the left lower quadrant when there were none in the right lower quadrant.

One dog was reopened 24 hours after intraperitoneal insertion of starch and no starch found. Consequently, a second dog was reopened at the same time, but plaques of starch and thin adhesions were found. This dog was then reopened in 4 days; starch plaques were still present, but had finally disappeared when opened in 6 days. The third dog was opened in 48 hours, and showed plaques of starch which had been absorbed when reopened in 5 days. The fourth dog was first opened in 72 hours and no starch could be found.

SUMMARY

Since the report by Antopol[1] in 1933, the dangers of talc implantation have been recognized. Granulomatous reactions, due to talc, result in intra-abdominal adhesions, persistent sinus formation, or nodules in the wound. Implantation of glove powder may occur from unwashed gloves, perforations in gloves, spill on to sponges, instruments, and suture material, and by the air-borne route. The frequency of such contamination is attested by the increasing numbers of case reports of serious complications due to talc. Animal experiments show that the granulomatous reaction can be regularly produced in the peritoneum, pleura, pericardium, muscle, joint, nerve, and tendon. The modified starch powder, No. 108, introduced by Lee and Lehman,[3] when placed in the same tissues by similar techniques is absorbed with little or no reaction.* Absorption by the dog peritoneum of 1 Gm. of starch apparently occurs within six days, but absorption of the same amount by the rabbit peritoneum is erratic.

CONCLUSIONS

1. Talc is a dangerous agent in its present use as a surgical glove lubricant.
2. A modified starch powder which is absorbed with little or no reaction is again suggested as a satisfactory substitute for talc.

*The few tiny starch granulomas found are felt to be due to the massive dose, and in time absorption would probably occur.

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A METHOD OF CONTINUOUS ARTERIAL INFUSION

Bone Marrow and Blood Levels During the Administration of Penicillin

S. Stanley Schneierson, M.D., and Lester Blum, M.D., New York, N. Y.

(From the Division of Bacteriology, Laboratories of The Mount Sinai Hospital)

A PREVIOUS investigation[1] revealed that substantial levels of penicillin could be obtained in the bone marrow of dogs following an intraarterial injection. The concentration was particularly high when two arterial injections, or an intravenous followed by an arterial injection, were made at an interval of some twenty or thirty minutes. In order to maintain constantly this high level, it was thought that a method of continuous arterial infusion might prove of advantage.

A satisfactory technique requires the injection of fluid in an even, measurable, and sterile fashion into a major artery against its high intraluminal pressure. The Brewer automatic pipetting machine was successfully adapted for this purpose.

APPARATUS

The apparatus (Fig. 1) consists essentially of a replaceable syringe (*E*) mounted on a motor-driven cam mechanism (*F*) which transfers fluid through an intake (*D*) and output (*C*) valve assembly from a glass container (*G*) into the artery (*A*). The machine is so designed that the volume delivered in any given period of time can be accurately regulated by three adjustments. These are the speed which can be controlled by a rheostat (*B*), the size of the syringe employed, and the length of thrust of each stroke. The latter is determined by the cam setting (*F*). That portion of the apparatus through which the fluid passes, namely, the glass container, tubing, valve assembly, and needle, is readily removable and can be sterilized as a unit. Good quality rubber tubing is used to connect the various parts. In general, No. 22 and 23 caliber needles are used. If small caliber needles are employed the flow from the needle is continuous in spite of the intermittent pumping action. When a small size syringe (*E*) is employed, in order to initiate the flow it is necessary to use an air bulb (*H*) to increase pressure in the bottle thereby forcing fluid into the tubing and wetting the valves. Once the flow is started, the pressure produced by the air bulb is no longer necessary.

MATERIAL AND METHODS

The experiments were performed on young, male dogs. The dogs were anesthetized by Veterinary Nembutal, administered intravenously. The dose was 0.5 c.c. per kilogram and, if necessary, more was administered during the operation.

Operation.—Under sterile conditions, the tibia and femur of one side were exposed, care being taken not to injure the nutrient vessels. The cortical layers of the presenting surfaces were chiseled off exposing the marrow cavities. Free bleeding was noted from the marrow, indicating an intact blood supply. Through a separate incision, the femoral vessels on the same side were also exposed.

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A 3 c.c. Luer-Lok syringe was employed and the machine adjusted to deliver 0.5 c.c. per thrust at the rate of 30 times per minute. At these settings, 15 c.c. can be delivered per minute thus requiring about thirty minutes for an infusion of 500 c.c. In some experiments the rate was altered as indicated in Table I.

Sterile physiologic saline solution, 500 c.c., was poured into the glass container to which was added the appropriate amount of crystalline sodium penicillin G. The system was primed with the air bulb and the machine was run momentarily until all the air bubbles were eliminated from the tubing.

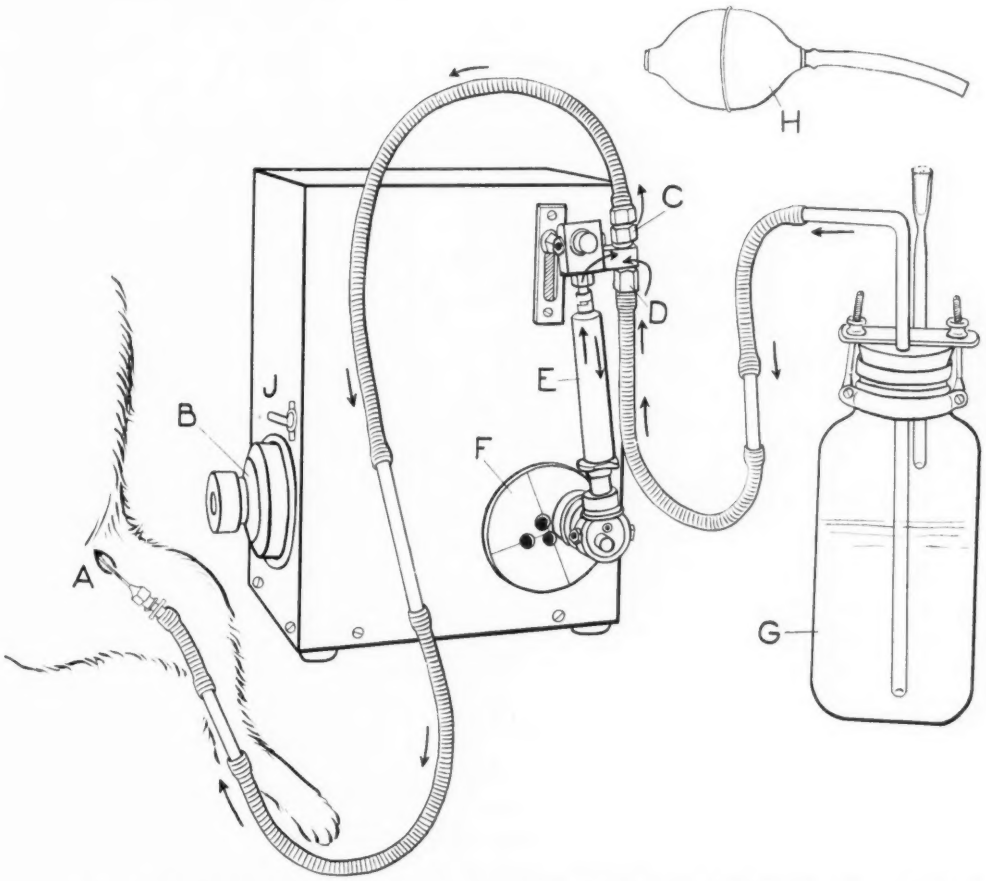

Fig. 1.—Apparatus for arterial infusion. *A*, Exposed femoral sheath with needle in femoral artery; *B*, rheostat to regulate speed; *C*, outflow valve; *D*, intake valve; *E*, Syringe; *F*, volume adjusting cam; *G*, glass bottle, *H*, air bulb; *J*, switch.

The needle was inserted through the exposed femoral sheath into the femoral artery. For technical and anatomic reasons, the needle was directed cephalad. The machine was then started and the infusion continued until the bottle was emptied. The level in the bottle was observed to drop steadily and progressively and there was no infiltration around the artery. At periodic intervals, specimens of the bone marrow were removed by a mastoid curette and simultaneous samples of blood from the marrow cavity, femoral vein, and some distant peripheral vein were obtained for comparison. At the conclusion of the infusion, the needle was withdrawn and bleeding stopped within a few seconds by firm compression.

TABLE I. PERIODIC LEVELS WITH CONTINUOUS VASCULAR INFUSION OF PENICILLIN IN DOGS

ROUTE OF INFUSION	ARTERIAL								VENOUS	
Total penicillin (in 500 c.c. saline)	40,000	100,000*	100,000	150,000	150,000	150,000	200,000	250,000	100,000†	200,000
Weight of dogs (kg.)	14.0	14.2	23.0	23.0	18.0	14.3	17.0	14.0	20.2	23.0
Duration of infusion (minutes)	20	30	40	20	30	40	30	20	30	30
Bone marrow (units per Gm.)										
10M	2.0	2.44	4.0	4.0	2.66	4.0	11.4	40.0	<0.55	0.88
20M	2.6	1.14	0.88	2.0	2.66	8.8	20.0	40.0	0.57	0.88
30M		8.8	4.0		4.0	11.4	16.0		0.57	0.88
40M			4.0			11.4				
Bone marrow blood (units per c.c.)										
10M	10.0	19.9	8.0	50.0	20.0		45.5	100.0	6.0	18.2
20M	8.0	23.5	10.0	13.3	40.0		50.0	>200.0	11.6	26.6
30M		24.3	13.0		40.0		45.5		9.0	26.6
40M			20.0							
Femoral vein (units per c.c.)										
10M	13.3	38.9	20.0		40.0		20.0	100.0	6.5	18.2
20M	20.0	28.2	20.0		50.0		45.5	66.6	11.6	26.6
30M		23.3	26.6				33.3		11.6	18.2
40M			–							
Peripheral vein (units per c.c.)										
10M	10.0	10.0	10.0		16.5		18.2		6.8	20.0
20M	8.0	11.4	20.0		25.0		26.6		11.6	20.0
30M		13.3	10.0				26.6		8.3	20.0
40M			20.0							

*Average of three dogs.
†Average of two dogs.

In control animals, the identical technique was employed except that the infusion was delivered into the femoral vein of the opposite side.

Penicillin Assays.—The method for assaying the bone marrow for penicillin was the same as previously described in detail.[1] Penicillin levels in the serum of the blood from the marrow cavity and the veins were determined in the usual fashion. The method of assay employed in this laboratory is a broth tube dilution method, using *Staphylococcus aureus II* as the test organism and fresh meat extract broth as the medium. The minimal concentration of penicillin required to inhibit an inoculum of 5 by 10^2 organisms was 0.02 units per cubic centimeter. The standard penicillin was obtained from the U. S. Department of Agriculture. All assays on the various specimens were accompanied by and compared with this standard.

PATHOLOGIC EXAMINATION OF THE INFUSED ARTERIES

In three dogs, six, twenty-eight, and forty-two days after infusion, respectively, the artery used was removed for examination. On gross examination, with the exception of the six-day specimen, the arteries appeared completely normal. The site of the injection of the six-day specimen was identified by the presence of a minute, organized clot on the surface of the puncture site.

Section of the arteries was made and stained with hematoxylin and eosin and with an elastic stain. On microscopic examination, the six-day specimen showed a plaque covering approximately $\frac{1}{6}$ of the circumference of the lumen,

which was confined only to this area. The elastica interna was interrupted and the intima over this area was swollen. The plaque contained small masses of eosinophilic material (fibrin ?) surrounded by fibroblastic proliferation. The media and adventitia were normal and no lesions were noted in the remainder of the circumference. No thrombosis was present in the lumen of the vessel. These changes were considered as being consistent with the normal reparative process. The twenty-eight and forty-six day specimens showed no change.

RESULTS AND DISCUSSION

The levels of penicillin in the bone marrow and in the blood from the various sites are recorded in Table I. As may be seen from this table, the concentration of penicillin in the bone marrow was considerably lower following intravenous than arterial infusion. The difference was especially marked when large doses were employed. Thus following the intravenous infusion of 200,000 units of penicillin over a period of thirty minutes, there were found 0.88 units of the drug per gram of bone marrow in samples taken at intervals of ten, twenty, and thirty minutes. In contrast, following arterial infusion of the same dose over the same period of time, the bone marrow showed concentrations of 11.4, 20.0, and 16.0 units per gram in samples taken at corresponding intervals. Good therapeutic effects may be anticipated from the high levels thus achieved in the marrow by means of an arterial infusion. Actually the method represents a modified form of direct instillation of the drug into the bone marrow supplied by the infused artery.

The data pertaining to blood penicillin values recorded in the table were analyzed from two points of view:

(1) Comparison of the levels found at the three different blood sites during any single arterial or intravenous infusion—In an arterial infusion, it may be noted that the penicillin values of the blood obtained from the marrow cavities of the femur and tibia (marrow blood) and from the femoral vein were considerably higher than the levels found in a distant peripheral vein. These findings are in accord with theoretical considerations since bone marrow blood is derived directly from the artery being infused and the femoral vein drains the treated extremity. Hence penicillin is constantly applied to these sites, whereas the blood in the peripheral vein is the result of dilution of the drug in the entire circulation. On the other hand, with intravenous infusion assay showed the levels to be the same at all three places at any given time. In this instance blood reaching the marrow and draining the extremity contains the same concentration of penicillin as the entire blood.

(2) Comparison of the levels achieved at any one site following arterial infusion with those found after intravenous infusion of the same amount of penicillin during the same period of time—Comparing the levels obtained by the different routes of administration, it may be seen that the values in the marrow blood and the femoral vein were considerably higher with arterial infusion than with intravenous infusion of the same amount of drug in the same period. With the arterial route, blood reaching these sites is being continuously charged with penicillin just prior to its arrival and hence has a higher concen-

tration. During intravenous infusion on the other hand, the blood reaching these points has the lower penicillin content of the general circulation. It was also found that the peripheral vein levels showed little or no difference regardless of the mode of administration provided the dose/time relationships were kept constant.

The rationale of the arterial administration of a therapeutic substance is based upon two objectives. One is the attainment of a comparatively high local tissue concentration relative to the amount injected. This can be achieved by infusion of the drug into the artery proximal to the organ in which it may be desirable to obtain a high level of the drug. The other is the minimization of any possible toxic effect by the interposition of a capillary field between the point of entrance of a drug into the blood stream and the vital organs.[2] The latter, although of not too great significance in the case of a substance as innocuous as crystalline penicillin, may prove to be extremely important if other drugs of greater toxicity are employed in the future. Thus the arterial method of administration may serve the purpose of producing maximal concentration in a given tissue with a minimal toxic effect. The chief advantage of continuous infusion over intermittent injections lies in the possibility of maintaining high concentrations over as long a period as seems desirable and thus diffusion into the tissue from the blood can be prolonged. By infusing directly into the blood supply of a particular tissue, the local concentration of penicillin in that tissue can be increased and maintained at an elevated level.

The chief technical problem in devising an apparatus for continuous arterial infusion is that of overcoming the high intraluminal pressure of an artery that gravity alone is unable to surmount. With the apparatus described in this report, this was readily accomplished. In addition, the apparatus was extremely simple, dependable, and the fluid was kept and delivered sterile. The entire technique is little more complicated than an intravenous infusion. The total amount delivered and the rate of administration may be easily controlled at all times.

It was noted during the course of the arterial infusion that an unusually large amount of blood oozed from the marrow cavity and the blood appeared more dilute than usual. This was interpreted as being due to an increase in the local blood volume. This phenomenon was not observed during the intravenous infusion.

The arterial infusion of penicillin caused no arterial damage. Immediate or delayed evidence of intimal irritation could not be demonstrated histologically. No difficulty was experienced in controlling bleeding after the needle was withdrawn provided the artery had not been denuded of the femoral sheath. The small hematoma formed within the sheath following the removal of the needle seemed to act as a tampon preventing further arterial oozing.

Bone marrow was selected for the tissue to be studied in this report for a number of reasons. The bone tissue is readily accessible for prolonged study and the artery supplying it directly may be conveniently used for infusion. Possible clinical application was also kept in mind. Although acute osteomyelitis usually responds to penicillin therapy,[3] the treatment of chronic osteomyelitis

by chemotherapeutic measures alone has not proved too satisfactory to date.[4, 5, 6] This failure has been attributed to the poor blood supply of the diseased bone as a result of pathologic process.[6] It is hoped that with this apparatus a higher concentration of the antibiotic can be delivered directly to the pathologic lesion for a longer period of time. In this way greater diffusion and penetration throughout the entire disease focus may ensue. A clinical trial of this technique is proposed.

We were greatly impressed with the practicability and ease of this method, the lack of evidence of any injury to the infused artery, and the ease with which bleeding from the artery can be controlled after the infusion.

SUMMARY

A satisfactory apparatus for continuous arterial infusion is described.

By means of this apparatus, penicillin in various doses was infused into the femoral artery, and then levels of the bone marrow of the femur and tibia and of the blood obtained from the marrow cavities, femoral vein, and a peripheral vein were determined. Suitable controls in which penicillin was administered intravenously were studied for comparison.

A high and constant level of penicillin was found in the bone marrow with continuous arterial infusion into the supplying artery. This was not achieved with intravenous infusion. Penicillin levels of the blood from the three sites studied were compared. With arterial infusion, it was noted that the penicillin levels of the blood from the marrow cavity and from the femoral vein were considerably higher than the general blood level. When administered intravenously, however, the penicillin levels at all three locations were about the same. It was also demonstrated that the arterial infusion of penicillin produced a much higher level in the bone marrow, blood, and femoral vein than the intravenous infusion of the same amount of drug in the same period of time. No significant differences in peripheral vein values could be shown by either route of administration. The theoretical basis for these results is discussed.

Examination of the arteries of three dogs, six, twenty-eight, and forty-two days after the arterial infusions showed no gross or microscopic abnormalities at the sites of administration. Although some changes were present in the six-day artery, these were considered within the scope of the normal reparative process.

We wish to express our gratitude to Dr. Gregory Shwartzman, Dr. Ralph Colp, and Dr. Sergei Feitelberg for their advice and encouragement. We are also thankful to Miss J. Jacowitz for her capable technical assistance.

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CARDIOCIRCULATORY DISTURBANCES DURING INTRATHORACIC SURGERY

CHARLES L. BURSTEIN, M.D., THOMAS L. PIAZZA, M.D., LOUIS A. KAPP, M.D., AND E. A. ROVENSTINE, M.D., BRONX, N. Y.

(From the Anesthesia Section of the Surgical Service and the Cardiac Section of the Medical Service of the Veterans Hospital)

THE purpose of this communication is to call attention to various cardiocirculatory disturbances, mainly reflex in nature, that may occur during intrathoracic surgery and to suggest some means of their effective management.

There have been at least three phases in the anesthetic management of thoracic surgery. The first phase comprised the development of techniques which resolved themselves in the establishment of efficient ventilation. The differential pressure chambers first devised soon gave way to the endotracheal technique[1] which was gradually modified by the application of controlled respiration[2] endobronchial intubation,[1] and compensated respiration.[3] A second phase devoted itself to proper fluid therapy in an effort to replace blood loss and to combat shock. The present phase is concerned with the study of various reflexes that may be produced from stimulation of the autonomic pathways and tissues rich in autonomic innervation which are present within the thoracic cavity in proximity to two of the more vital organs, the heart and lungs.

In previous studies it was indicated that cardiac arrhythmias, particularly during cyclopropane anesthesia, could be prevented and corrected by the intravenous injection of procaine hydrochloride.[4] It was later observed that acute arrhythmias occurring while intrathoracic surgery was being completed during Pentothal sodium and ether anesthesia could also be relieved by intravenous procaine.[5] The respective advantages of both controlled respiration and compensated respiration were presented.[3] Cardiovascular derangements due to mechanical causes such as positional changes and the use of chest rests were pointed out.[6] Various intrathoracic vagal reactions have been observed and treated either by local procaine infiltration or by blocking the vagus nerve itself.[3] Observations in a large Thoracic Surgery Center during World War II called attention to the severe cardiovascular reactions incident to manipulation of pathologic pericardium; these cardiovascular reactions were more severe than those observed during myocardial or intracardiac interventions.[3]

In the present study, a group of thirty-three intrathoracic procedures were thoroughly studied for reflex cardiovascular derangements throughout the various phases of surgical intervention by means of the electrocardiogram as well as by continuous blood pressure and pulse rate determinations. The operations consisted of eight pneumonectomies, seven lobectomies, three pericardiectomies, nine transthoracic vagotomies, one transthoracic gastrectomy, three mediastinal tumors, and two exploratory thoracotomies.

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All known precautions and treatment regarding preoperative preparation, physiopharmacologic antagonism, respiratory control, circulatory control, and fluid therapy were carefully employed. Six out of thirty-three of the patients operated upon showed no significant cardiovascular changes throughout surgical intervention. These were two pneumonectomies, two lobectomies, one vagotomy, and one mediastinal tumor. In eight other cases, transient circulatory changes occurred only at the time of endotracheal intubation.

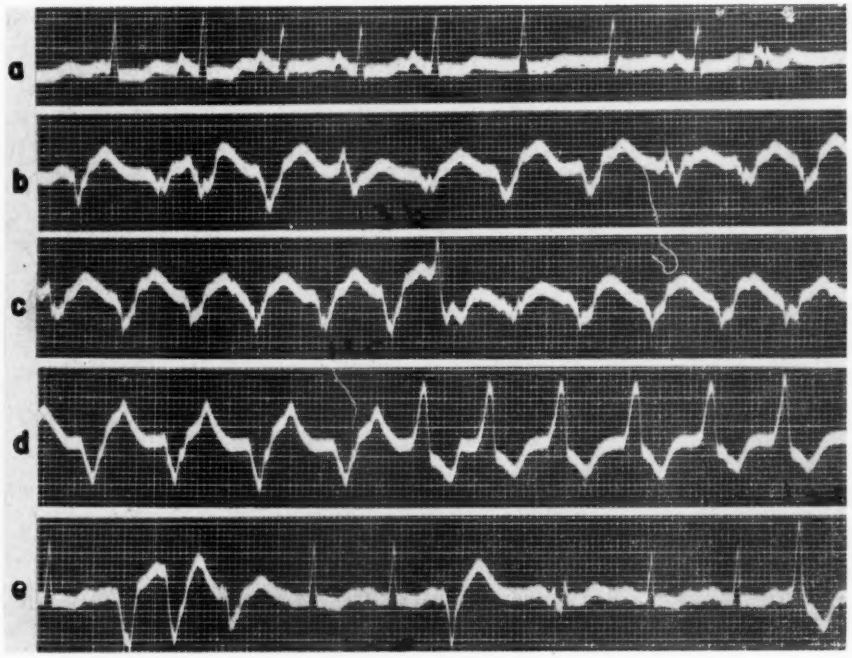

Fig. 1.—Electrocardiographic changes during pericardial manipulation. *a*, During cutting of the pericardium the pacemaker shifted to a nodal rhythm. *b*, *c*, *d*, Eight minutes later, paroxysmal ventricular tachycardia followed by occasional ventricular extrasystoles were recorded. *e*, After the intravenous injection of 100 mg. procaine there was a return to the sinus rhythm.

A certain number of patients demonstrated cardiovascular changes incident to various manipulations. Those which occurred more frequently were circulatory reactions which coincided with the following procedures: pericardial manipulation, pleural incision, endotracheal intubation, vagus nerve stimulation, pulmonary hilar or bronchial manipulation, rib periosteal scraping, intercostal nerve stimulation, and positional changes during anesthesia.

Effects of Pericardial Manipulation.—Every one of the three patients who sustained a pericardiectomy demonstrated marked cardiovascular changes when the pericardium was being manipulated or stripped. This corroborates previous findings in a series of 121 cardiac or paracardiac operations of which 47 were pericardial, which showed that the pericardial operations were the ones most prone to manifest severe cardiovascular disturbances.[3, 5] Intracardiac manipulations or operations on the myocardium were tolerated with comparatively less severe circulatory changes. The three cases in this series exhibited cardio-

vascular changes which could be detected clinically as acute arrhythmias by means of pulse palpation and sphygmomanometry.

Electrocardiographic tracings in the first pericardiectomy showed that during dissection of the adhesive pericardium there was a transition from a sinus rhythm to a nodal rhythm (Fig. 1, *a*). The pulse felt irregular and 100 mg. of 1 per cent procaine solution were injected intravenously. Eight minutes later, paroxysmal ventricular tachycardia was recorded (Fig. 1, *b*). At this point, the peripheral pulse felt bizarre. Again 100 mg. of procaine were injected intravenously and this was followed by a return to a normal pulse and the electrocardiogram showed a return to a sinus rhythm (Fig. 1, *c*, *d*, and *e*).

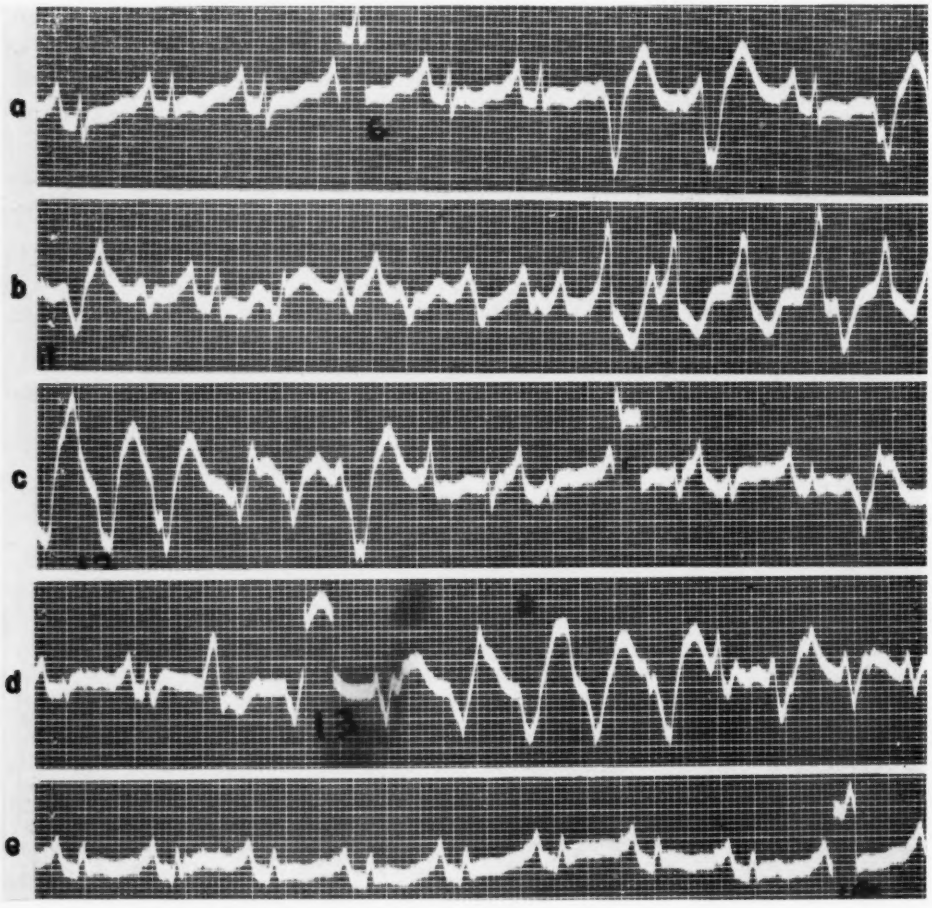

Fig. 2.—Electrocardiographic changes during pericardial manipulation. *a*, Initial pericardial manipulation resulted in ventricular extrasystoles. *b*, *c*, *d*, Continued manipulation of pericardium resulted in paroxysm of ventricular tachycardia. *e*, Sinus rhythm returned after procaine was injected intravenously and manipulation ceased.

In the second pericardiectomy, a rapid and irregular pulse became manifest immediately following the first manipulations of the pericardium. The electrocardiogram showed numerous ventricular extrasystoles at this point (Fig. 2, *a*). Procaine, 100 mg., was injected intravenously and procaine solu-

tion was applied topically to the pericardium. After this, the pericardium was manipulated and stripped for eight minutes with the maintenance of a regular sinus rhythm. During subsequent cardiac manipulation, ventricular tachycardia developed (Fig. 2, *b*, *c*, and *d*). At the time of the last acute arrhythmia 50 mg. of procaine were again injected intravenously. This was followed by a return to a regular sinus rhythm which maintained thereafter (Fig. 2, *e*).

In the third pericardiectomy, procaine in 5 per cent concentration was applied topically and 50 mg. of a 1 per cent solution were injected intravenously. The cardiac disturbances consisted of runs of ventricular premature systoles. At another point there were frequent multifocal premature ventricular contractions with runs of idioventricular rhythm.

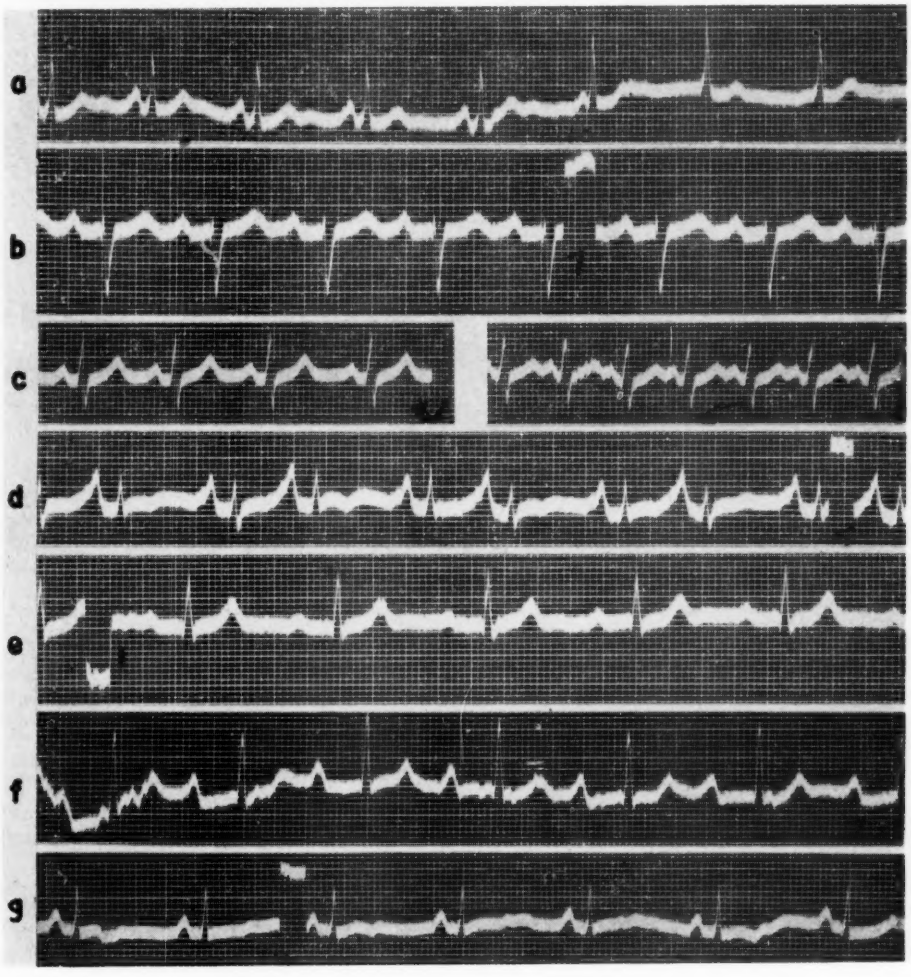

Fig. 3.—Electrocardiographic changes during pleural incision. *a*, Nodal rhythm developed during pleural incision. *b*, Sinus rhythm with P-R interval prolongation. *c*, Sinus tachycardia; rate 150 (second strip) as pleura was incised. Immediate prior rate (first strip) was 100. *d*, Auricular extrasystoles of bigeminal type. *e*, A-V conduction defect (P-R interval prolongation). *f*, A-V block with increased P-R interval from 0.24 to 0.32 seconds. *g*, Low and diphasic T waves. Regular sinus rhythm.

Effects of Pleural Incision.—Seven patients (over 20 per cent) showed significant electrocardiographic changes at the time when the pleura was being incised. One patient (Case 3, a pneumonectomy) developed a nodal rhythm (Fig. 3, *a*). Another (Case 9, a lobectomy) showed delay in A-V conduction (Fig. 3, *b*). One (Case 10, a lobectomy) developed a sinus tachycardia at a rate of 150 from a previous rate of 100 (Fig. 3, *c*). One (Case 17, a pericardiectomy) developed auricular extrasystoles of bigeminal type (Fig. 3, *d*). One patient (Case 19, a vagotomy) showed A-V conduction defect (Fig. 3, *e*). One (Case 26, a vagotomy) manifested A-V block with increased P-R interval (Fig. 3, *f*). Another (Case 32, an exploratory thoracotomy) manifested low and diphasic T waves (Fig. 3, *g*).

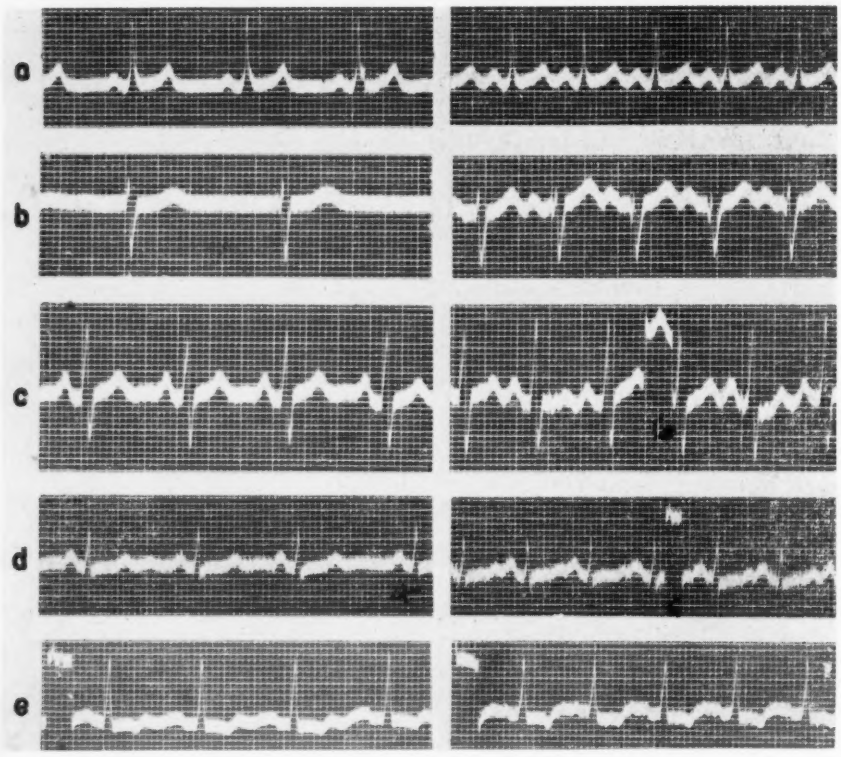

Fig. 4.—Development of sinus tachycardia during endotracheal intubation. In each case from *a* to *e* the first strip represents the tracing before intubation. The second strip shows the effect at intubation.

Effects of Endotracheal Intubation.—There was a high incidence (73 per cent) of electrocardiographic changes which occurred at the time the endotracheal tube was introduced. These changes were transient and were not perceived clinically. The most frequent change (in sixteen) was the development of a sinus tachycardia which doubled the previous cardiac rate of 60 or 80 to 120 to 150 (Fig. 4, *a* to *e*).

A nodal rhythm developed in two cases (Fig. 5, *a* and *b*). One patient manifested A-V conduction defect (Fig. 5, *c*). In one case the voltage of the

T waves became lower (Fig. 5, *d*). Two patients developed ventricular extrasystoles and shifting pacemaker (Fig. 5, *e*). Sinus bradycardia, from 95 to 55, occurred in one case (Fig. 5, *f*).

One patient who was intubated awake following laryngeal and tracheal cocainization developed paroxysmal tachycardia at a rate of 170. General anesthesia was then induced with cyclopropane and ten minutes later the electrocardiogram showed a regular sinus rhythm at a rate of 80 (Fig. 5, *g*).

Effects of Vagus Nerve Stimulation Including Pulmonary Hilar Traction and Bronchial Manipulation.—It is known that stimulation of the vagus nerve

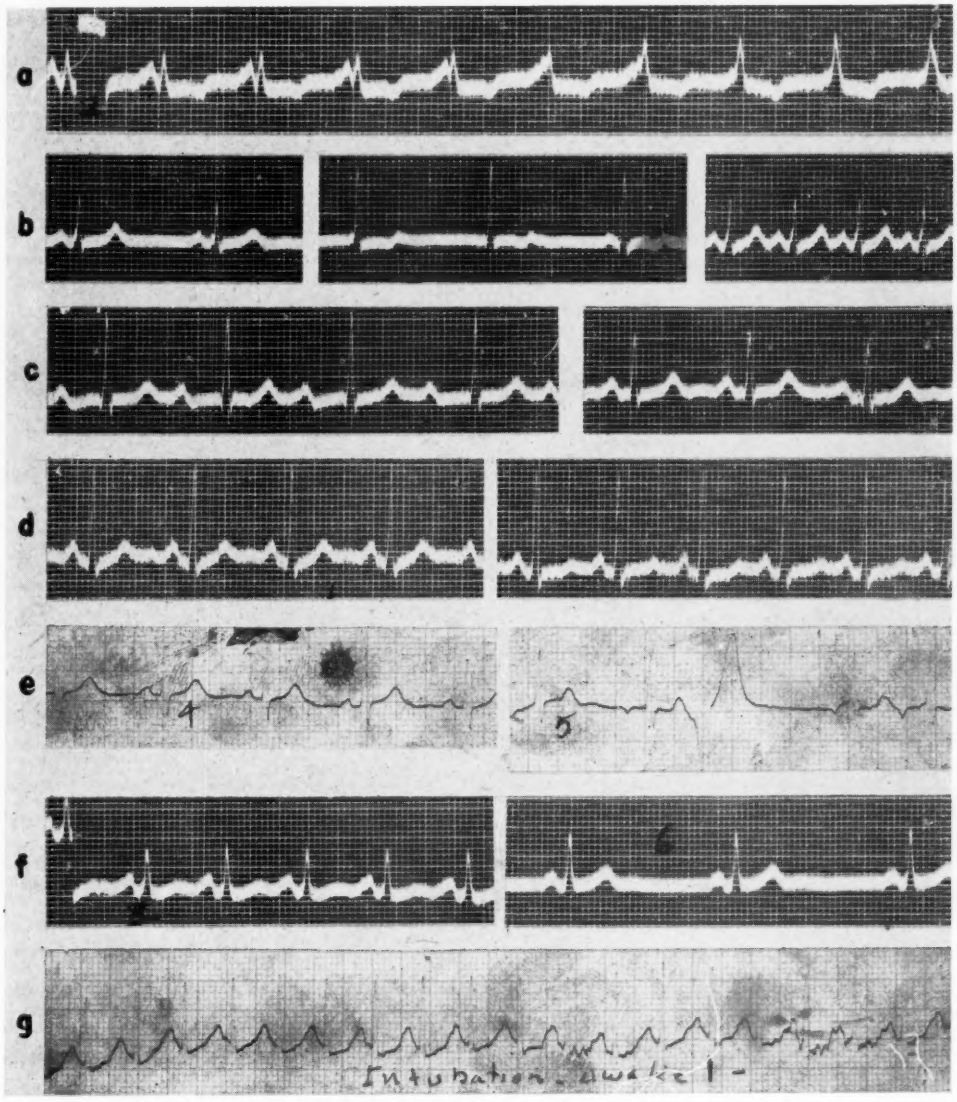

Fig. 5.—Other electrocardiographic changes during endotracheal intubation. *a*, Nodal rhythm. *b*, First strip: sinus rhythm prior to intubation; second strip: nodal rhythm during intubation; third strip; sinus tachycardia one minute after intubation. *c*, First strip: immediately following intubation, A-V conduction defect (P-R interval prolonged to 0.28 seconds); second strip: ten minutes after intubation, the P-R interval returned to 0.16 seconds). *d*, T waves show decreased voltage. *e*, Ventricular extrasystoles; shifting pacemaker. *f*, Sinus bradycardia. *g*, Supraventricular paroxysmal tachycardia.

in the chest, at or above the heart level, is apt to cause cardiovascular changes. Manipulation about the pulmonary hilum or of a main bronchus is also known frequently to cause cardiovascular reactions of the vagal stimulation type.

In this series only six cases out of thirty-three exhibited such effects, all of which were mild and transitory. Case 19 (a vagotomy) showed A-V conduction defect (Fig. 6, *a*) when each vagus nerve was manipulated before section just above the diaphragm. One patient (Case 10, a lobectomy) developed a sinus bradycardia of 60 (Fig. 6, *b*) when the hilum was being manipulated.

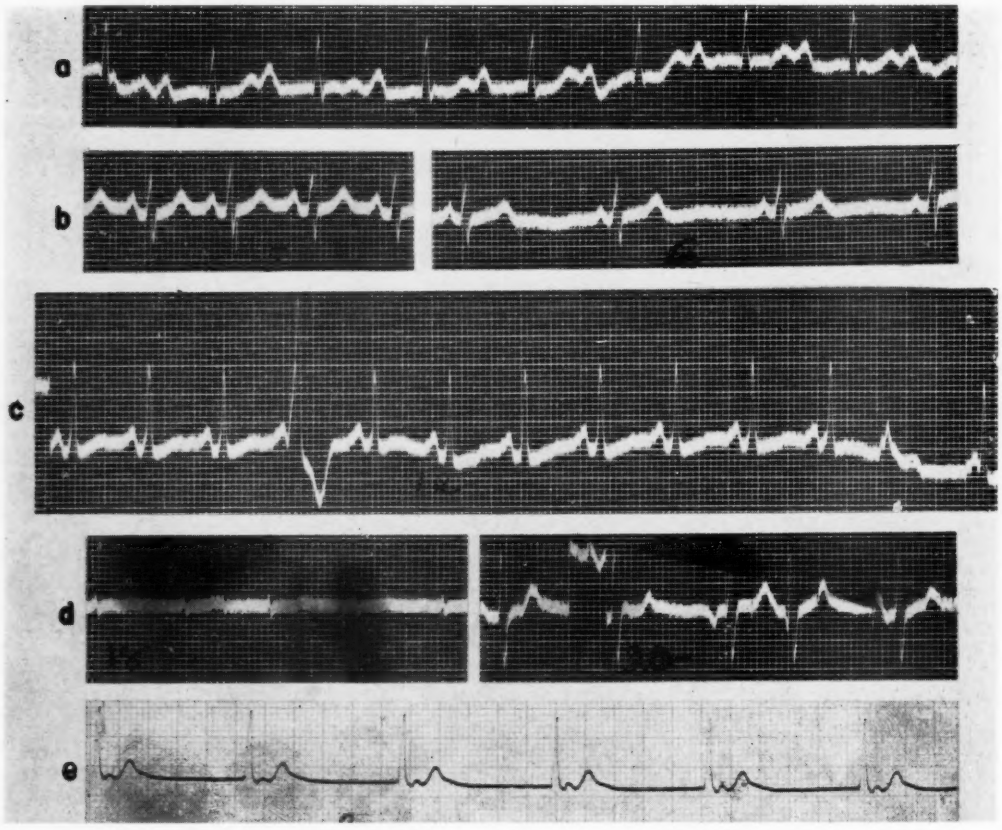

Fig. 6.—Electrocardiographic changes during vagus nerve stimulation or pulmonary manipulation. *a*, A-V conduction defect during vagotomy. *b*, Sinus bradycardia during manipulation of pulmonary hilum. *c*, During cutting of a bronchus, there developed a decrease in the voltage of the T Waves, depression of S-T segment and ventricular premature contractions, one of which was interpolated. *d*, Manipulation of a bronchus resulted in low voltage QRS complexes and T waves (first strip) and nodal escape followed by nodal extrasystoles (second strip). *e*, Nodal rhythm during dissection of pulmonary hilum.

During the cutting of the bronchus of one patient (Case 3) the electrocardiogram showed the development of T waves of low voltage, depressed S-T segment, and ventricular premature contractions, one of which was interpolated (Fig. 6, *c*). In Case 4, when a bronchus was being manipulated there occurred low voltage QRS complexes and T waves; later, there was nodal escape followed by nodal extrasystoles (Fig. 6, *d*). One patient (Case 6, a pneumonectomy) developed a nodal rhythm when the hilum was being dissected (Fig. 6, *e*). Another (Case 20, a vagotomy) showed blood pressure changes during mani-

pulation of the vagus characterized by a fall in arterial blood pressure from 150/100 to 100/80 mm. Hg with a decrease in pulse pressure to 20. Five minutes later, the blood pressure was 160/145 (with a pulse pressure of only 15). The pulse rate during this period decreased from 100 to 80 per minute while extrasystoles could be palpated at the pulse. Electrocardiographic tracings at this time showed occasional ventricular extrasystoles. After both vagi were cut the pulse became regular and the blood pressure leveled off at 120/70.

It is believed that vagal reactions in this series which comprised nine vagotomies were minimal for two reasons: (1) Procaine solution was always injected into the vagus before manipulating or cutting it. The posterior pulmonary plexus was likewise injected with procaine solution when the hilum was to be dissected or manipulated. (2) The vagotomies were done by cutting the vagi low in the chest, one to two inches above the diaphragm. Experimental findings have shown that the vagus in this region is less sensitive to afferent stimuli.[7] Stimulation of the vagus at the level of the heart or higher in the chest, on the contrary, is the most sensitive portion of the vagus and ordinary mild stimuli may provoke marked hypotension and asystole.[7]

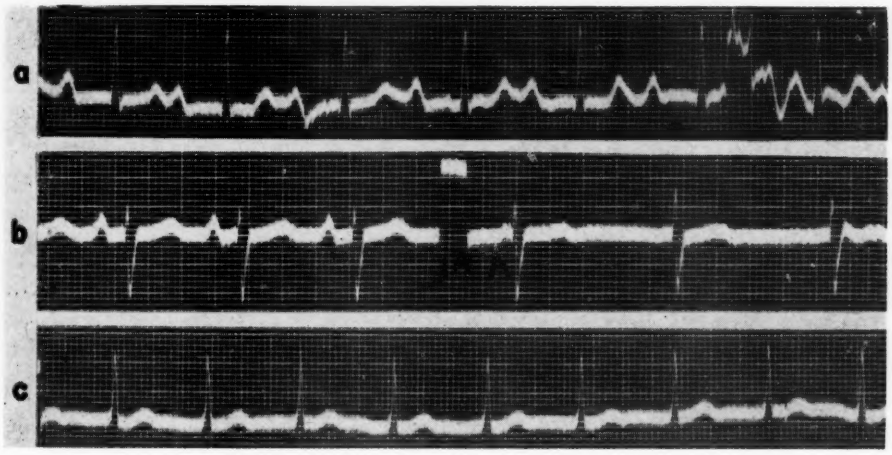

Fig. 7.—Electrocardiographic changes incident to rib scraping and intercostal nerve stimulation. *a*, A-V conduction defect (first degree heart block) when rib periosteum was being scraped. *b*, Nodal rhythm during the crushing of an intercostal nerve, rate 60 per minute. *c*, Nodal rhythm during rib scraping, rate 95 per minute.

Effects of Rib Scraping and Intercostal Nerve Stimulation.—Occasionally, stimuli of rib scraping or intercostal nerve manipulation resulted in cardiovascular changes indicative of vagal disturbance. One patient (Case 19) developed an A-V conduction defect (Fig. 7, *a*) when rib periosteum was being scraped. Another (Case 9) developed a nodal rhythm (Fig. 7, *b*) when an intercostal nerve was crushed. One (Case 3) also developed a nodal rhythm when the ribs were being scraped (Fig. 7, *c*).

Effects of Positional Changes.—Cardiovascular changes incident to changing the position of an anesthetized patient from the supine to the lateral position were occasionally observed.

In Case 32, turning the anesthetized patient onto the good side resulted in a fall of blood pressure from 140/90 mm. Hg to 80/60. This hypotension

was maintained until the pleura was opened, at which time the blood pressure rose to above its normal systolic and pulse pressures (Fig. 8). It may be recalled that these positional blood pressure changes are greatly enhanced when

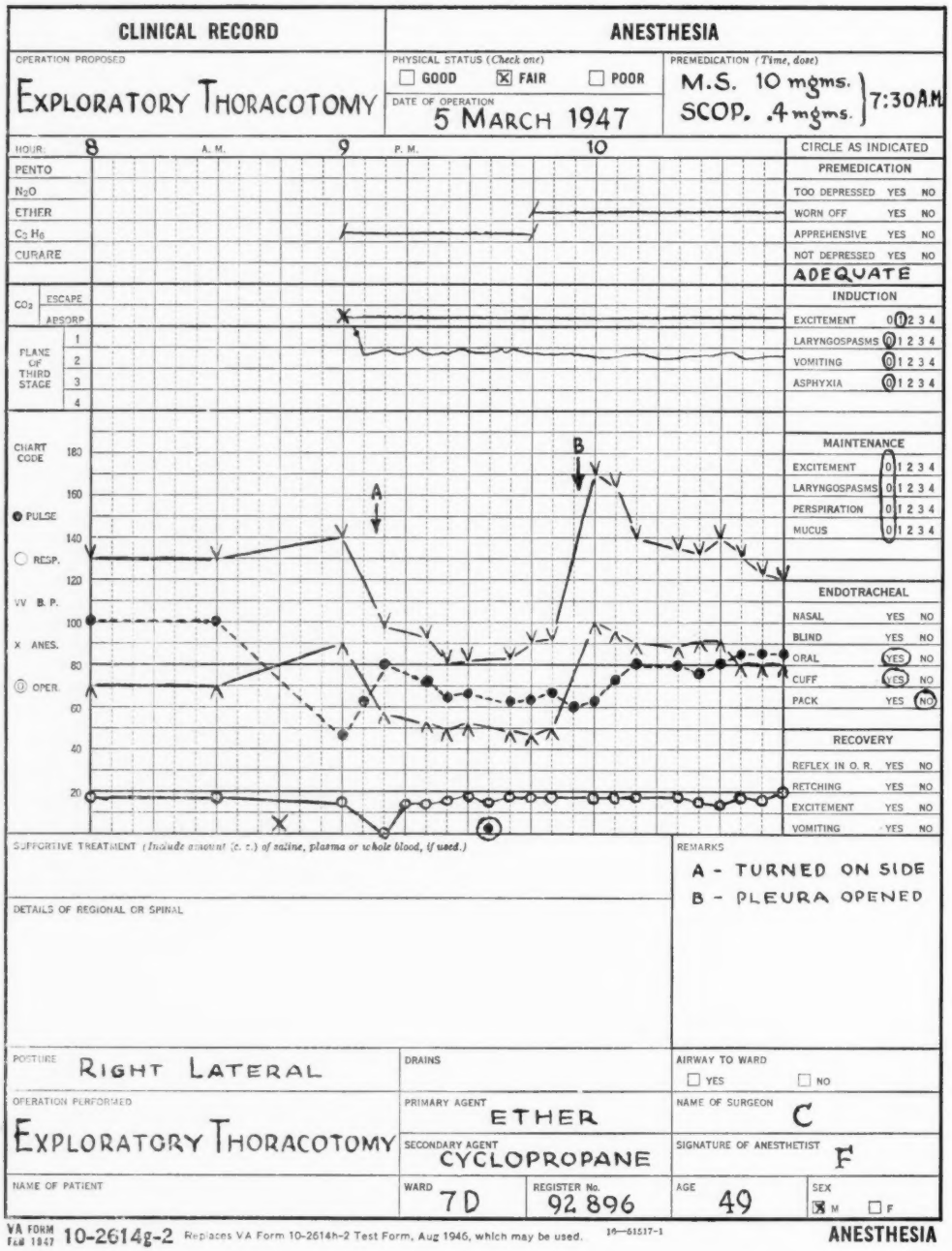

Fig. 8.—Postural hypotension. Turning the anesthetized patient onto the good side resulted in a fall of the arterial blood pressure from 140/90 mm. Hg to 80/60 (*A*). This hypotension was maintained until (*B*) when the pleura was opened, at which time the apparent cardiac tamponade was released and the blood pressure rose to above its normal systolic and pulse pressures.

an anesthetized patient is turned from the supine to a lateral position complicated by the application of a chest elevator. This latter device was shown to constrict so mechanically the contents of the chest that tamponade of the heart and/or the great vessels could ensue.[3]

A similar hypotension following the changing of the anesthetized patient from the supine to the lateral position occurred in Case 27 in which the blood pressure fell from 130/70 to 90/64 and the hypotension lasted 25 minutes. An electrocardiographic tracing taken immediately after turning the patient showed a sinus tachycardia at a rate of 120 in contrast to the previous rate of 70.

DISCUSSION

From the foregoing study several recommendations may be deduced:

No chest elevator was used in the present series of cases and severe positional cardiovascular changes of the cardiac tamponade type were not observed. However, significant and sustained arterial hypotension did occur in a number of cases when they were turned from the supine to the lateral position after previous anesthetization. To obviate this type of cardiovascular disturbance it was deemed advisable to *place the patients in the operative position from the outset* and to induce anesthesia and perform tracheal intubation in that position. Laryngoscopy in a patient lying on his side may seem awkward when first attempted but this technique is quickly mastered and the operator appreciates the freedom of the patient's head which can be flexed or extended to the position which permits optimal laryngoscopy.

The high incidence (73 per cent) of cardiac irregularities which occurred at the time an endotracheal tube was passed should be considered. Further intensive studies are now in progress to determine the various conditions and mechanisms involved in these derangements. Precursory examination of the material at hand would seem to indicate that the cardiac abnormalities induced at the time of tracheal intubation are produced by a *reflex* mechanism since the arrhythmias occur at the very instant that the tube is introduced. Reid and Brace described a reflex arrhythmia under similar conditions and concluded that it was a "vagovagal" reflex with signs of cardiac vagal stimulation characterized by bradycardia, delayed conduction time, and extrasystoles—both auricular and ventricular.[8] In the present study, a reflex of sympathetic stimulation was more frequently encountered. In any case, since a reflex phenomenon is involved, the recommendation to be made at the present time to mitigate these reactions is to attempt intubation of the trachea at a fairly deep plane of anesthesia, preferably in the third plane.

Rib and intercostal nerve stimulation occasioned by periosteal rib scraping, direct intercostal nerve stimulation prior to rib resection, and wide rib spreading by rib retractors may cause cardiovascular changes characterized by A-V conduction defect, nodal rhythm, and arterial hypotension. A simple and effective means to prevent such abnormalities is to inject the affected intercostal nerves with a local anesthetic solution. If the local anesthetic agent used is one of long duration it will enhance its utility by minimizing postoperative pain.

Pleural incision was attended by significant electrocardiographic changes in over 20 per cent of the cases. None of these was severe but if one is to avoid untoward reactions in debilitated individuals or in patients with pre-existing cardiac pathology, it would be advantageous to apply a local anesthetic agent topically upon the surface of the pleura prior to incising it.

Circulatory reactions due to vagal stimulation from manipulation of the hilar pulmonary plexus or from direct mechanical pressure upon the vagus nerve in the chest are characterized by arterial hypotension and bradycardia. These effects can be easily abolished by the local infiltration in the affected area of 5 to 10 c.c. of 1 per cent procaine solution and by minimizing the mechanical stimulation.

Manipulation or incision of pathologic pericardium, particularly inflammatory pericardium, is usually attended by the severe cardiocirculatory reactions noted during the course of the three pericardiectomies just described. Topical application of 2 per cent procaine solution as well as rapid intravenous injection of 100 mg. of procaine solution in a 1 or 2 per cent concentration are recommended. It is believed that such procaine therapy tends to overcome cardiac hyperirritability due to pericardial and cardiac manipulation during the phase of general anesthesia.

SUMMARY

Electrocardiographic and sphygmomanometric determinations during thirty-three intrathoracic interventions have revealed numerous areas which, when stimulated even during general anesthesia, are apt to produce reflex cardiocirculatory disturbances.

The most common areas of such reflex disturbances were observed during endotracheal intubation, following positional changes under anesthesia, during rib periosteal scraping and intercostal nerve stimulation, at the time of pleural incision, during pericardial manipulation, and during vagus nerve stimulation.

A discussion of the prevention of these cardiocirculatory disturbances and of their treatment when they occur is presented.

The authors wish to thank the various members of the Cardiac and Anesthesia Services as well as the members of the Medical Illustration Department for their technical assistance.

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THE OCCURRENCE OF THE GAS STOPPAGE SENSATION IN ACUTE OBSTRUCTION OF THE ILEUM

E. LAWRENCE KEYES, M.D., ST. LOUIS, MO.

(From the Department of Surgery, St. Louis University Medical School, and from the St. Louis City Hospital)

PAIN (1) begins in the middle of the abdomen, (2) accompanied by a downward urge, and (3) persists despite defecation for hours at the onset of acute obstruction of the ileum. Pain with these characteristics is associated with the gas stoppage sensation. After some hours vomiting occurs, and certain of these characteristics ordinarily disappear. This study will be limited to the early hours of pain prior to vomiting.

ILLUSTRATIVE CASE PRESENTATIONS

The characteristics of the pain of onset will be studied as they appeared in the case histories of the six patients with acute obstruction of the ileum. Obstruction arose internally, caused by strangulating intraperitoneal bands or by volvulus of the ileum, in four of the patients; obstruction arose externally, in strangulated inguinal or femoral hernias, in two of the patients. The ileum was found gangrenous at operation in four of the patients, resection of the ileum being performed; the ileum was found viable at operation in two of the patients.

CASE 1.—Mrs. N. G. (St. Louis City Hospital, No. 41781), aged 34 years, was admitted May 6, 1945. The chief complaint was "bellyache" of forty-eight hours' duration.

Illness Upon Admission.—About forty-eight hours before, pain began feeling "like you'd eaten green apples" about the umbilicus. For relief the patient took several laxatives and two enemas, but that did not relieve the condition. There had been no defecation since the day before onset, and anorexia since onset. After fourteen hours of persisting pain, vomiting began, first food recently eaten, later fecal. She vomited twenty-five times in all. The parumbilical pain persisted, and pain was referred also to the back.

Previous History.—Pelvic laparotomy.

Physical Examination.—The patient looked sick. A midline suprapubic scar was seen on the abdomen. There was slight distention and generalized tenderness of the abdomen increasing toward the right lower quadrant, where a soft mass could be felt; there was no rebound tenderness or rigidity.

Roentgenograms were interpreted to show small bowel distended by gas with fluid levels.

White blood cell count was 2,600 without shift; temperature was 100° F., pulse 60, respirations 26, blood pressure, 100/70.

Diagnosis.—Acute obstruction of the small bowel.

Laparotomy.—Acute obstruction of the ileum was found, with gangrenous strangulation of the ileum from peritoneal bands. The gangrenous portion of ileum was resected with primary anastomosis.

Result.—The patient recovered.

Comment.—In this typical example of acute strangulation obstruction of the ileum, the initial pain was associated with the gas stoppage sensation because (1) pain began in the midline of the abdomen (parumbilical); (2) accompanied by a downward urge, evident because of the taking of laxatives and enemas;

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and (3) pain persisted despite enemas for fourteen hours before vomiting occurred.

CASE 2.—Mrs. P. A. (St. Joseph's Hospital, Alton, Ill.), aged 58 years, was seen in October, 1947.* The chief complaint was pain in the abdomen of thirty-one hours' duration.

Illness Upon Admission.—Shortly after supper the day before, sudden severe pain began, generalized throughout the abdomen, and accompanied by an urge to defecate so strong that, during the next seven hours, the patient took three enemas and a suppository. Vomiting occurred about 1½ hours after onset. During the next fourteen hours pain abated to some extent, though never disappeared completely. Suddenly the pain increased, again accompanied by a violent urge to defecate, and followed by nausea and vomiting. The pain was rhythmical, with periods of exacerbation lasting for three minutes.

Physical Examination.—There were two consultations. At the first consultation seven hours after onset, the abdomen was found tender throughout but not distended, and with no increase in peristaltic sounds. White blood cell count was 10,000 without shift; temperature was 98.6° F.

At the second consultation, thirty-one hours after onset, tenderness was found localized at McBurney's point; there was no distention or accentuation of the peristaltic sounds. White blood cell count was 12,000 with shift.

Diagnosis.—Acute condition of the abdomen, most likely acute appendicitis, but possibly due to acute obstruction of the terminal ileum.

Operation.—Volvulus of the terminal ileum was found with peri-appendicitis. The volvulus was untwisted.

Result.—The patient recovered.

Comment.—The initial pain was associated with the gas stoppage sensation in this patient, and the downward urge was violent.

Before operation the diagnosis of acute appendicitis was made, although the diagnosis of acute obstruction of the ileum was also considered. At operation the latter diagnosis proved correct and volvulus of the ileum was found.

The gas stoppage sensation regularly occurs in two acute conditions of the abdomen, namely in acute appendicitis,[1] and in acute obstruction of the ileum.[2] It is usually absent in other acute conditions of the abdomen.

CASE 3.—Mr. E. W. (St. Louis City Hospital, No. 52542), aged 35 years, was seen Dec. 11, 1945.† The chief complaint was "stomach-ache" of nine hours' duration.

Illness Upon Admission.—Cramping generalized pain began in the abdomen at 5 A.M. thought by the patient "due to gas." In attempts at relief the bowels moved at 9 A.M. Despite defecation pain persisted. He vomited twice, beginning at 2 P.M.

Previous History.—There had been a similar attack two years before.

Physical Examination.—The patient appeared in acute distress. The abdomen was distended without any intestinal pattern. The bowel sounds consisted of rushes in the right upper quadrant. The abdomen was diffusely tender without rebound tenderness. Rectal examination was normal.

Roentgenograms showed small bowel distended with gas.

White blood cell count was 12,000 with shift; temperature was 96° F., pulse 68.

Diagnosis.—Acute intestinal obstruction.

Laparotomy.—Operation showed volvulus of the terminal ileum without gangrene. The volvulus was untwisted.

Result.—The patient recovered.

Comment.—This patient with acute obstruction of the ileum from volvulus was seen early in the attack, that is, about nine hours after onset. At that time

*I am indebted to Dr. Gordon Moore for this case history.

†I am indebted to Dr. M. Hara for this case history.

the picture of acute obstruction of the ileum seemed clear-cut, the diagnosis being, in part at least, attributable to the presence of the gas stoppage sensation and to the familiarity of Dr. Hara with the significance of the sensation.

Note the persistence of the initial pain in the midline of the abdomen despite defecation. Persistence of pain despite defecation is a characteristic of the gas stoppage sensation, illustrated by this patient.

CASE 4.—Mr. W. S. (St. Louis City Hospital, No. 38232), aged 66 years, was seen Jan. 27, 1945. The chief complaint was pain in the epigastrium for fifteen hours.

Illness Upon Admission.—Pain began in the epigastrium, beltlike in distribution, and accompanied by a desire to defecate. Pain persisted for eight hours, and there was nausea but no vomiting.

Physical Examination.—The patient looked sick. The abdomen was entirely normal to physical examination, with no distention, tenderness, or spasm, and no abnormal bowel sounds noted. White blood cell count was 12,000 with shift.

Diagnosis.—A definitive diagnosis was not made at this time, eight hours after onset.

Second Consultation.—By the time of the second consultation, seven hours later, and fifteen hours after onset, vomiting had occurred, vomitus containing blood clots and bile. No defecation had occurred since onset.

Physical Examination.—The abdomen was tender and rigid throughout with rebound tenderness. Rectal digital examination was normal.

Roentgenograms showed loops, probably small bowel, distended with gas.

Diagnosis.—Acute obstruction of the small bowel.

Laparotomy.—Gangrene of several feet of terminal ileum from strangulation by peritoneal bands was found. Resection was done by the resident, with primary anastomosis.

Result.—The patient died on the third postoperative day.

Comment.—Before the diagnosis of acute strangulation obstruction of the ileum was definitely established, this patient was seen twice in consultation. The first consultation was held eight hours after onset. There was a history of pain associated with the gas stoppage sensation, followed by nausea but no vomiting. The abdomen was entirely normal to examination. The leucocyte count was 12,000. A diagnosis was not definitely made at this time.

The second consultation was held seven hours later, that is fifteen hours after onset. Vomiting had occurred meanwhile. Signs had appeared in the abdomen. The x-ray film was reported to be suggestive of small bowel obstruction. A definite diagnosis of acute small bowel obstruction was made at this time. Operation was performed. The ileum had become gangrenous and was resected. The patient died.

Early diagnosis would perhaps have been made had I exhibited greater confidence in the reliability of the gas stoppage sensation than I did.

CASE 5.—Mr. W. R. (St. Louis City Hospital, No. 39659), aged 64 years, was seen March 5, 1945. The chief complaint was (1) parumbilical pain of thirty-six hours' duration and (2) pain in hernia of thirty-six hours' duration.

Illness Upon Admission.—"Yesterday the [right femoral] hernia was sore," the patient stated. "I took a drink of water and then had a kind of [parumbilical] hurting. I tried to defecate but could do nothing. The bowels moved for the last time two days ago. I sat on the stool quite a bit." The parumbilical pain persisted, increasing in severity. Twenty-four hours after onset he ate and vomited immediately afterward for the first time, with some relief of pain. Again he tried to defecate, and again could not, but vomited in-

stead, vomitus consisted of food just eaten. The abdominal pain persisted, and the cycle of eating, downward urge, and vomiting was repeated several times.

Previous History.—The patient had had a similar attack seven weeks before.

Physical Examination.—The patient appeared sick and dehydrated. There was moderate distention of the abdomen below the umbilicus and "stepladder phenomenon," with tenderness and rigidity in both lower quadrants. A right femoral hernia was tender and irreducible. White blood cell count was 17,350 with shift. Temperature was 100° F., pulse 96.

Diagnosis.—Strangulated right femoral hernia.

Operation.—Gangrenous ileum in a strangulated femoral hernia was found. The loop was resected with primary anastomosis.

Result.—The patient recovered.

Comment.—The diagnosis of strangulated femoral hernia was obvious in this patient. One might therefore be inclined to disregard the symptoms in the abdomen.

Nevertheless, study of the initial symptoms in the abdomen prove instructive, for they are the same, with ileum strangulated externally, for instance in this patient, as with ileum strangulated internally, for instance in the preceding patients.

This patient, for example, felt pain beginning in the midline of the abdomen (parumbilical), accompanied by a downward urge evidenced by attempts at defecation; and pain persisted for twenty-four hours before vomiting occurred. Here, as in the preceding patients, pain began associated with the gas stoppage sensation.

CASE 6.—Mrs. G. S. (St. Louis City Hospital, No. 41307), aged 64 years, was seen April 24, 1945. The chief complaint was vomiting for six days.

Illness Upon Admission.—The attack began six days previously. Right after supper severe cramps began radiating from the right upper quadrant to the hypogastrium, simultaneously with a "rising" in a right inguinal hernia. Two hours later she had an urge to defecate but could not. Next she drank water and vomited, and thereafter "every time I drank water I vomited" she observed, the vomiting being repeated frequently during the six days. During this time no bowel movement occurred.

Previous History.—A right inguinal hernia had been present for three years.

Physical Examination.—The patient appeared sick and dehydrated. There was much distention of the lower abdomen with "stepladder phenomenon," tenderness, and rebound in both lower quadrants, especially the right. A right inguinal hernia was irreducible, though not tender. White blood cell count was 6,600, temperature 99° F., pulse 88.

Diagnosis.—Strangulated right inguinal hernia.

Operation.—A gangrenous loop of ileum was found strangulated in the right inguinal hernia. Resection of the loop with primary anastomosis was performed.

Result.—The patient recovered.

Comment.—Although vomiting may overshadow other symptoms during the latter portion of the clinical picture of acute obstruction of the ileum, as it did here, nevertheless the onset may prove characteristic. Here, for instance, vomiting had continued for six days, the patient suffering from strangulation of a right inguinal hernia. Nevertheless, prior to vomiting, during 5½ hours pain in the abdomen had been accompanied by a strong downward urge.

DISCUSSION

The six patients of this series each had acute obstruction of the ileum. The pain of each was similar at onset, for (1) pain began in the midline of the

abdomen (epigastrium, parumbilical, hypogastrium, or generalized: (2) accompanied at first by a downward urge, evident from the taking of enemas or laxatives, from trips to the toilet, or from defecation at an unusual time; and (3) pain persisted despite defecation and despite enemas for ten hours, on the average, before the occurrence of vomiting.

The pain of each patient, therefore, began associated with the gas stoppage sensation. This sensation was present in the patients having internal obstruction of the ileum.

The initial pain of every patient persisted for hours, the average time being 10 hours, the shortest 1½ hours, the longest 24 hours before the occurrence of vomiting.

Persistence of pain was present in every patient. In none was pain intermittent. Pain-free intervals did not occur, although there occurred variations in intensity of pain.

LITERATURE

"Pain is the essential symptom" in acute obstruction of the ileum, Richardson[4] wrote in 1932; "pain of a cramp-like or continuous character persisting in spite of enema."

This sentence contains most of the points of the present paper.

The downward urge was alluded to by Wangensteen[5] and by Fitz.[6]

SUMMARY

Pain is associated with the gas stoppage sensation when (1) pain begins in the midline of the abdomen, (2) accompanied by a downward urge, and (3) persisting despite defecation for hours.

This syndrome occurs in acute obstruction of the ileum before the occurrence of vomiting.

The syndrome occurs in acute appendicitis before localization of pain in the right lower quadrant of the abdomen.

A patient seen, for example, eight hours after onset with this syndrome is to be suspected of having one or the other of the two aforementioned diseases, even though the abdomen is soft, and even though vomiting has not occurred. Obviously, no accepted diagnostic aid (such as auscultation, rectal digital examination, leucocyte counts, and other laboratory aids, especially scout film of the abdomen) is to be neglected in making the correct and early diagnosis.

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FOREIGN BODY IN THYROID FOLLOWING PERFORATION OF ESOPHAGUS

EDWARD E. JEMERIN, M.D., AND JACOB S. ARONOFF, M.D.
NEW YORK, N. Y.

(From the Surgical and Rhinolaryngological Services of The Mount Sinai Hospital)

THREE instances in which an unusual sequence of events followed perforation of the esophagus by a foreign body have been encountered at The Mount Sinai Hospital, New York, N. Y., since 1941. In all, clinical and roentgenographic evidence of cervical and retroesophageal infection developed and external cervical drainage was performed. The findings, however, were at variance with the perdominantly retro- or paraesophageal infection usually found. Instead, the infection was chiefly confined within one of the lateral lobes of the thyroid gland, embedded within which was also found the foreign body. The perforation had apparently taken place more or less directly into the lateral thyroid lobe.

Study of the literature has revealed no similar cases. To list the large number of negative references would be pointless, but a thorough review to 1941 can be found in Neuhof and Jemerin's monograph on *Acute Infections of the Mediastinum*. Suffice it to say that in none of the reports before or since that date has this particular variation of foreign body perforation of the esophagus been described. Moreover, the first of our cases required a secondary exploration to retrieve the foreign body because the true sequence of events had not been appreciated at the first operation. For these reasons it is felt that our cases and the special features of this variant should be reported.

CASE 1 (Mt. Sinai Hospital No. 471866).—F. D., a woman 73 years of age, was admitted April 15, 1941, with an eight-day story of dysphagia and fever following the swallowing of a chicken bone. On admission the temperature was 101.4° F. The trachea was in the midline and freely movable. Tenderness was present along the right sternomastoid and anterior to this muscle there was more marked tenderness with the suggestion of a mass low down in the neck. The lower teeth were in bad condition and there was a full upper plate. A plain film of the neck revealed a 3 cm. linear foreign body in the soft tissues just anterior to the fifth and sixth cervical vertebrae with moderate widening of the prevetebral soft tissues. A soft tissue mass was seen on the right side at the root of the neck extending to just below the jugular notch. The cervical trachea was compressed and slightly displaced to the left by this mass which had the appearance of an enlarged thyroid.

On the day of admission, right cervical exploration was performed.* Extensive edema of the periesophageal tissues was noted but no pus was encountered in the retroesophageal space. The right lobe of the thyroid was seen to be enlarged and pale and suggested fluctuation. It was aspirated and thick foul yellow pus was obtained. A large cavity was then entered and evacuated from within the substance of the thyroid gland. The foreign body was not found. The cavity was packed and a light packing was also placed down to the retroesophageal space. On culture of the pus *Streptococcus hemolyticus B, Streptococcus viridans A, and Staphylococcus albus B* were obtained. Anerobic cultures were not done.

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*By Dr. A. S. W. Touroff.

Following this the temperature dropped to a lower level but since the foreign body had not been retrieved, esophagoscopy was done two days later. The foreign body was not found in the esophagus. Marked edema of the hypopharynx and upper introitus was present and a perforation of the posterior wall at the level of the cricopharyngeus muscle, with pus exuding from it, was seen. X-ray examination on April 16, 1947, showed some increase in the retrotracheal and retropharyngeal widening with air trapped within. The foreign body, with some air about it, was lying undisturbed as at the previous examination. On April 18, the temperature began to rise again and the x-ray examination was repeated after administering a barium swallow and placing two metal clips into the wound as markers. This showed the upper esophagus displaced forward by soft tissue swelling with a perforation measuring about 0.5 cm. in the posterior wall at the level of the foreign body. None of the barium escaped into the tissues about the foreign body, suggesting that the perforation was closed off. The foreign body lay behind this barium-filled cavity and in front of the metal clip markers.

Fig. 1*A* (Case 2).—Plain lateral film of neck, Oct. 31, 1941, showing foreign body, slight retrotracheal widening, and a few air streaks in retrotracheal space (arrow points to foreign body).

The neck was explored secondarily on April 18.* A small cavity containing about 3 c.c. of intensely foul pus was evacuated behind the esophagus at the level of the perforation. The original cavity in the thyroid was then carefully re-examined and a chicken bone about one inch in length, with its long axis vertical, was found in its anterior limit and removed. The cavity was packed. A small esophageal perforation was demonstrated in the posterior cervical esophageal wall by methylene blue. It should be noted that the foreign body, while

*Also by Dr. Touroff.

shown to be posterior to the esophagus in the roentgenogram, was nevertheless within the cavity in the thyroid gland. This was possible because the esophagus was displaced forward by retroesophageal infection, a feature demonstrated both roentgenographically and at operation.

The postoperative course was entirely satisfactory. The temperature became normal by the fourth postoperative day, and a Levine tube which had been inserted at operation was removed on this day. The patient was discharged twelve days following the second procedure (April 30, 1941) with a small superficial granulating wound and no evidence of an esophageal leak. In follow-up study on July 15, 1941, the wound was well healed and the patient symptom free.

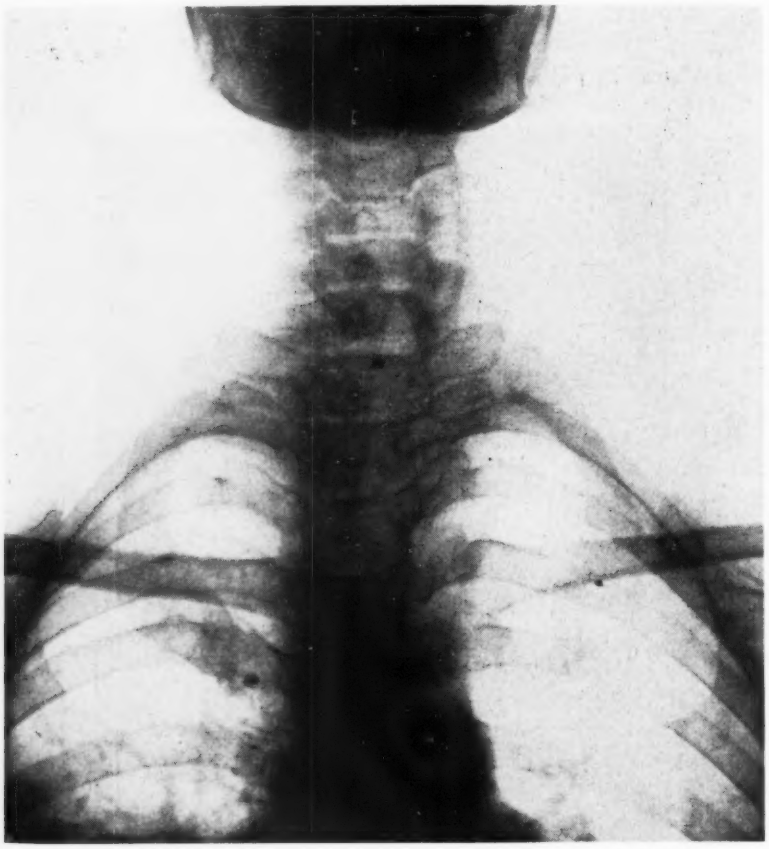

Fig. 1*B* (Case 2).—Nov. 2, 1941, displacement of trachea to left.

CASE 2 (Mt. Sinai Hospital No. 481176).—T. O. was a 58-year-old woman admitted on Oct. 31, 1941.* She gave a history of having swallowed a chicken bone the day before admission. This was followed by pain in the neck and marked dysphagia to the extent of being unable to retain any food. On admission the temperature was 100° F. and there was tenderness in the region of the right lobe of the thyroid gland. There was also moderate edema of the right arytenoid. Esophagoscopy upon admission showed two small puncture wounds covered with exudate in the esophagus just below the cricopharyngeus. Roentgenogram of the neck (Fig. 1*A*) showed a linear density about the level of the cricoid extending across the region of the esophagus, and slight widening of the retrotracheal space at the level of the cricoid.

*A private patient of Dr. Joseph A. Goldman, to whom we are indebted for permission to use the case.

The following day the temperature rose to 102.6° F. and continued irregularly up to this level until operation on November 7. The tenderness in the region of the right lobe of the thyroid became more marked and esophagoscopy and x-ray examination were repeated on November 2. On this day esophagoscopy showed some bleeding in the region of the puncture wound but no pus or foreign body was found. The film showed the linear density situated somewhat more horizontally than before and there was questionable increase in the widening of the retrotracheal space. Left lateral deviation of the trachea was also seen (Fig. 1*B*). Additional roentgenograms were taken on November 3, 4, and 6 (Fig. 1*C*). Each showed the position of the foreign body as before and slight but progressive increase and further caudal extension of the widening of the retrotracheal space. The widening did not, however, extend down into the superior thoracic aperture. Another esophagoscopy, on November 6, showed purulent secretion emanating from the region of the punctures of the right upper esophagus. Localized tenderness over the right thyroid lobe, dysphagia and edema of the right arytenoid persisted, and some fullness over the right lobe of the thyroid was noted.

Fig. 1*C* (Case 2).—Nov. 6, 1941, definite increase in retrotracheal widening which, however, does not descend to superior thoracic aperture (arrow points to foreign body).

On November 7 exploration of the neck with removal of the foreign body and drainage of an abscess of the right lobe of the thyroid were performed.* The approach was the usual cervical approach anterior to the border of the right sternomastoid muscle. The esophagus was exposed and the retroesophageal space entered, but only edema was encountered there. The right lobe of the thyroid seemed enlarged. It was aspirated and thick yellow odorless pus was obtained. An abscess in the lobe itself was then entered and found to contain about

*By Dr. Touroff.

1 dram of pus. Cultures were not made. Within the abscess cavity, the chicken bone was found and removed. It measured about 1½ inches. Methylene blue given by mouth failed to appear in the wound either because the communication between the esophagus and the cavity was too long and narrow, or because the tract had sealed off spontaneously. The abscess cavity was packed and two small packings were placed down to the superior mediastinum. The skin was loosely closed around the packings.

The postoperative course was uneventful except for fixation of the right vocal cord in the cadaveric position and slight accompanying dysphagia. The temperature became normal by the fourth day after operation and remained so until the patient's discharge on Nov. 15, 1941. The dysphagia and local tenderness also disappeared promply after operation.

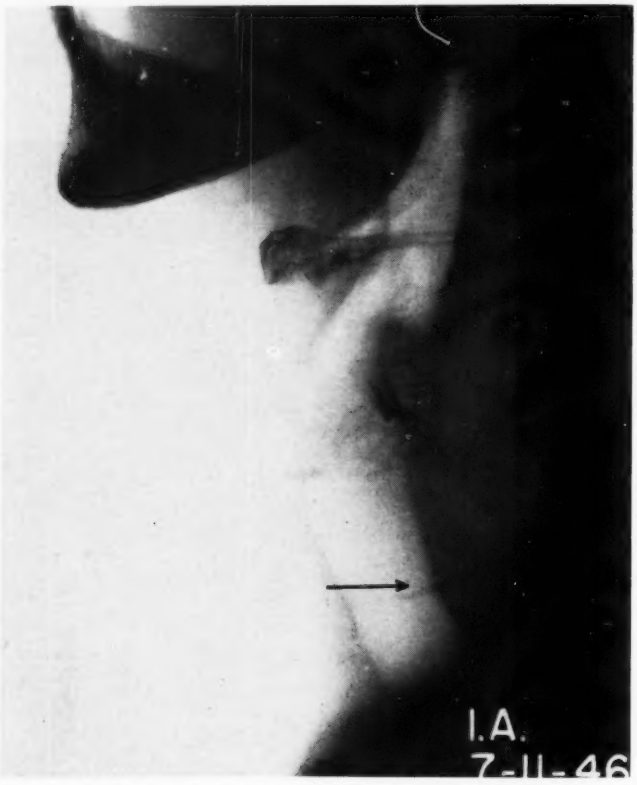

Fig. 2 (Case 3).—July 11, 1946, lateral film of neck showing foreign body and retrotracheal widening (arrow points to foreign body).

CASE 3 (Mt. Sinai Hospital No. 551425).—I. A., a 61-year-old woman, was admitted on July 11, 1946, with a history of having experienced sudden pain and dysphagia while eating carp three weeks before admission. She visited a physician that same night who sent her to a hospital where she was examined and discharged immediately. No roentgenographic studies were made. Pain and dysphagia persisted for one week and the patient consulted another physician who again told her nothing was wrong. The symptoms increased in intensity and during the week prior to admission were associated with the development of a swelling over the left side of the neck. The past history was entirely negative.

Examination on admission revealed an indurated swelling beneath the left sternomastoid muscle which seemed to be in continuity with the left lateral lobe of the thyroid gland. The swelling was moderately tender. The trachea seemed pushed forward somewhat although the retrosternal space was not entirely obliterated. The patient seemed anxious, apprehensive, and acutely distressed. She was edentulous except for four lower incisors. Laryngoscopic

examination showed pale swellings of both arytenoids with some pooling of mucopus behind them. Esophagoscopy showed no swelling of either pyriform fossa. The esophageal mucosa was slightly edematous and one plaque of exudate was seen on the posterior wall below the cricopharyneus. No foreign body or perforation was seen. The temperature was 100.6° F. A roentgenogram of the neck showed widening of the retrotracheal space extending down to the superior thoracic aperture. The fishbone was seen in the lateral view at about the level of the sixth cervical vertebra. It was perpendicular to the long axis of the esophagus and extended across and anterior to it being in large part, if not entirely, outside of it (Fig. 2). The trachea was seen to be displaced to the right in the posteroanterior film. Because of the experience in the previous two cases, perforation into the left lateral lobe of the thyroid was considered. This clinical impression was borne out at operation, performed on the night of admission (E. E. J.). An incision was made along the anterior border of the left sternomastoid which was seen to be edematous. The muscle was retracted along with the structures of the carotid sheath. The middle thyroid vein and omohyoid muscle were divided. The lateral lobe of the thyroid was swollen and bulged into the wound. The normal sulcus between it and the esophagus was obliterated by a thick pyogenic membrane. The superior mediastinum was packed off and this membrane was then bluntly opened, entering a cavity containing about one ounce of putrid pus. The pus was evacuated and the cavity examined. It extended from between the esophagus and the lateral lobe of the thyroid into the lateral lobe where its major component lay. The esophagus was much thickened. Careful examination of the esophagus and retrotracheal space revealed no foreign body and no perforation was demonstrated by inspection or by methylene blue given by mouth. Palpation of the cavity within the thyroid lobe revealed the fishbone in the lobe itself. The bone was removed and the cavity, retroesophageal space, and superior thoracic aperture were loosely packed. Culture of the pus from the abscess cavity was positive for *Staphylococcus aureus A*. Anerobic studies were not done.

The patient was given penicillin and sulfadiazine and was fed parenterally for two days after the operation. The temperature was normal by the fourth postoperative day. The course was entirely smooth and the patient was discharged two weeks after operation with a small superificial granulating wound.

She was seen in follow-up study in September of the same year, at which time the wound was well healed and pliable and she had no complaints.

DISCUSSION

These three cases comprise a hitherto undescribed sequence of events following foreign body perforation of the cervical esophagus, namely, the passage of the foreign body into the thyroid gland with the formation of an abscess within the thyroid as well as or instead of the customary periesophageal abscess. Most perforations of the cervical esophagus take place posteriorly at the pharyngoesophageal junction because of the sudden narrowing at this site, the change of direction, and the V-shaped area in the posterior esophageal wall at this level where the outer longitudinal layer of muscle fibers is lacking. The buccopharyngeal fascia is closely applied to the posterior wall of the esophagus and the perforating agent usually perforates this as well, entering the retrovisceral space where the customarily ensuing infection then develops.

Apparently, however, perforation does also occur in a lateral or even anterolateral direction, although this seems less likely when an instrument is the agent than in the case of a foreign body. In such an instance the foreign body can make its way directly into the corresponding lateral lobe of the thyroid gland. Conceivably, even a foreign body perforating posterolaterally might find its way into the thyroid gland if its course after perforation was

lateral or anterolateral. This is what probably occurred in Case 1 where a posteriorly situated perforation was seen endoscopically, although this might have represented instead a secondary evacuation site of the undrained retroesophageal abscess.

The infection which follows develops not only paraesophageally but in the thyroid lobe as well. If the course has been directly into the thyroid with minimal traversal of the retroesophageal space, the infection may be entirely or chiefly within the gland. In Case 1, the infection was chiefly within the gland, only a small retroesophageal component being found at the secondary operation. In Case 2 the infection was confined entirely to the gland; at operation only edema was found in the retroesophageal space. In Case 3 the abscess cavity was both paraesophageal and intraglandular.

Characteristically, the infection should be anerobic with putrid odor, and liquefaction with abscess formation should be the rule. Phlegmonous extension should occur if drainage is too long delayed, but apparently this is more characteristic of perforation into the retroesophageal plane than when the dense confines of the thyroid have been penetrated. An abscess was the pathologic lesion in all three of our cases; the infection was putrid in two, odorless in one (Case 2).

In all the cases the foreign body was found entirely within the thyroid gland. Whether the initial vis a tergo carried it there, or whether the subsequent swallowing and gagging movements did, cannot be said. It should be noted that an edentulous, plated upper jaw probably predisposes to the ingestion of foreign bodies since the customary discriminatory sensation is eliminated from this area. This was mentioned by Myerson. Two of the patients reported upon wore upper plates; in the third no record was made, although in view of the patient's age it is likely that she also did.

Diagnosis of esophageal perforation with paraesophageal infection is not difficult. A history of the ingestion of a foreign body followed by neck pain, dysphagia, and fever is usually obtained. The physical signs are those of an inflammatory process in the neck consisting of tenderness, mass, and fixation or displacement of the trachea. With perforation into the thyroid the swelling and tenderness may be largely confined to the corresponding lateral thyroid lobe, which may suggest the specific diagnosis, as in Case 3. Esophagoscopy may be of assistance in demonstrating that a perforation has occurred. A lateral roentgenogram of the neck is indispensable. This will usually show the foreign body and air trapped in a widened retrotracheal space. The frontal film may show lateral tracheal displacement. There apparently is not as great a tendency in these cases for infection to travel down the retrovisceral compartment into the superior mediastinum as when perforation has taken place into that compartment. This is manifested by tapering of the retrotracheal widening in the direction of the superior thoracic aperture.

Treatment consists of the establishment of external drainage through the neck and removal of the foreign body. The operation should be performed under local anesthesia. The technique, patterned after Marschik, is now well-standardized. It is described in detail in Neuhof and Jemerin's monograph.

There should be no mortality. Chemotherapy will not substitute for surgery and has a place only after adequate drainage has been effected.

It is important to retrieve the foreign body during the procedure as otherwise relief may prove to be only temporary, as in Case 1. Unless definite search is made with the finger within the cavity in the thyroid gland, the foreign body may be missed as its location makes it difficult or impossible to bring it into the field of vision. The experience in Case 1 was instrumental in guiding the search in Cases 2 and 3 into the cavity in the thyroid gland where the foreign body was located.

SUMMARY

1. Three cases of an unusual variety of foreign body perforation of the cervical esophagus are reported.

2. In each, the course of the foreign body was through the esophagus into the thyroid gland in which it became embedded.

3. Contamination of the retrovisceral space was minimal. The resultant infection, an abscess in each case, was predominantly within the corresponding lateral thyroid lobe.

4. The variations of this type of lesion and its treatment are discussed.

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FURTHER STUDIES ON THE EFFECT OF CONTINUOUS INTRAGASTRIC INFUSION OF ACID AND PEPSIN IN DOGS

M. J. Fogelman, M.S., M.D., M. I. Grossman, Ph.D., M.D., and A. C. Ivy, Ph.D., M.D., Chicago, Ill.

(From the Department of Clinical Science, University of Illinois College of Medicine)

INTRODUCTION

WHILE there is no satisfactory evidence to show that hypersecretion of gastric juice is the primary cause of the disease peptic ulcer, a wealth of evidence has implicated acid and pepsin as a sine qua non for the development of the clinical and experimental lesion. However, certain important questions concerning the relationship of acid and pepsin to the genesis of peptic ulcer still remain unanswered. Can acid-pepsin alone in physiologic amounts and concentrations produce ulcerative changes in the gastroduodenal mucosa? How long must the gastroduodenal mucosa be exposed to what concentration of acid-pepsin in order that ulceration result? To what extent does pepsin enhance the injurious action of acid gastric juice? This work represents an attempt to offer partial answers to these basic questions.

The literature dealing with the role played by acid and pepsin in the pathogenesis of peptic ulcer has recently been reviewed by Cummins, Grossman, and Ivy.[1] Three main methods have been employed to study the effects of acid and pepsin on the gastrointestinal mucosa. These are the perfusion technique, sham feeding, and histamine administration. In summary of these methods the following may be said. First, results with perfusion techniques with acid or acid-pepsin have demonstrated the injurious action of these solutions on the gastrointestinal mucosa under the unphysiologic conditions employed (to be described later). Second, no experiments have offered definite proof that hypersecretion resulting from intermittent sham feeding can produce ulceration. Results obtained by the few workers who reportedly obtained ulceration of the gastroduodenal mucosa have not been reproducible. Third, the histamine-induced ulcer may be partially the result of angiotoxic and cytotoxic effects of the drug, with hypersecretion as a cooperating injurious agent which digests an already damaged mucosa.

THE PROBLEM

In 1948, Cummins, Grossman, and Ivy[1] studied the effect of intragastric administration of 0.10N hydrochloric acid on the gastroduodenal mucosa. Animals receiving hydrochloric acid per gastrostomy continuously developed acute perforating ulcers in from forty to ninety hours. These animals also developed a metabolic acidosis. When they repeated the experiments giving equal amounts of acid, but also protecting the animal against acidosis by the parenteral administration of sodium bicarbonate, none of the animals developed ulcers, even if

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acid was continuously administered for twelve days. Hence, their work disclosed the interesting fact that acid alone, for the period of observation, was not ulcerogenic, provided there was no change in the acid-base balance of the animal and demonstrated, which would seem obvious, the unnatural conditions of all previous experiments on this topic.

The problem then arose as to whether the addition of pepsin or an increase in the acid concentration would lead to ulcer formation. This study, therefore, was undertaken to determine what effect the continuous intragastric infusion of acid pepsin solutions would have on the gastroduodenal mucosa.

METHODS

The methods employed were essentially those of Cummins, Grossman, and Ivy.[1] Healthy male and female mongrel dogs were used. All animals were kept in individual cages for a period of observation ranging from four to eight days preceding the onset of the experiment.

Gastrostomies were performed under aseptic conditions with the animal anesthetized with nembutal. From five to seven days later, the animal was lightly anesthetized with ether or nembutal, the gastrostomy opened, and a plastic cannula inserted into the left external jugular vein. Following the insertion of the gastrostomy tube and vein cannula, the animal was immediately prepared for continuous intragastric and intravenous infusion. In order to administer fluids intravenously it was necessary to use a method of restraining the animal so that it could not have access to the delivery tubes or indwelling catheters. Binders made of mattress ticking were tailored to fit each animal. Four lightweight chains were attached to the binders, one above each leg. The animals were then placed in a cage and each chain was fixed to a corresponding corner of the cage. In this way the animal was allowed to sit up or stand, but was prevented from turning around or from rolling over on its back or extreme sides. By means of rubber tubing the vein cannula and gastrostomy tube were connected to graduated flasks placed above and outside the cage.

0.10N acid-pepsin solution was made by adding 2 Gm. of pepsin* to one liter of isotonic 0.10N HCl. Using the hemoglobin substrate method, the solution yielded a peptic activity of 23×10^{-4} units. 0.15N acid-pepsin was made by adding the same amount of pepsin to one liter of 0.15N HCl.

Blood pH determinations were performed on arterial blood drawn from the femoral artery under anaerobic conditions into a silicon greased syringe containing 0.2 c.c. of a heparin-fluoride solution. The pH of the whole blood was immediately determined by using a MacInnes glass electrode mounted in a constant temperature chamber (37.5° C.), and measuring with a Cambridge pH meter.

All animals were fed commercial dog food† once daily. Control and treated animals were run in scattered distribution so that both groups were exposed to approximately the same environmental conditions. Three groups of animals were run as follows.

*Merck & Co., Inc., Rahway, N. J.
†Pard.

Series I (Controls).—Five dogs. These animals were subjected to continuous intragastric infusion of 0.10N HCl-pepsin per gastrostomy. The solution was instilled at a rate of 9 to 10 c.c. per kilogram body weight per hour, which usually amounted to 2,000 to 2,600 c.c. per dog per twenty-four hours. These animals were sacrificed in from forty-eight to eighty-four hours, at which time they were moribund.

Series II.—Fourteen dogs. These animals also received continuous intragastric infusion of 0.10N acid-pepsin, but in addition, 0.16N $NaHCO_3$ was simultaneously administered intravenously. The rate of administration of bicarbonate was presumptively determined by the amount necessary for in vitro neutralization of equal amounts of acid-pepsin, and more definitely by the amount necessary to maintain the blood pH at normality as indicated by daily pH readings. This amounted to from 2.9 to 5.0 c.c. per kilogram body weight per hour of 0.16N $NaHCO_3$ with an average value of 4 c.c. per kilogram per hour. Acid-pepsin was infused at a rate of 9 to 10 c.c. per kilogram of body weight per hour. Dogs in this group were autopsied at various periods ranging from four to eleven days.

Series III.—Fourteen dogs. In these animals 0.15N acid-pepsin was continuously infused intragastricly and neutralization was effected by the intravenous administration of 0.30N $NaHCO_3$. Acid pepsin was given at a rate of 9 to 10 c.c. per kilo body weight per hour and the bicarbonate administered in quantities necessary to maintain the blood pH at normality as determined by daily pH readings. From 3.7 to 5.1 c.c. (average 4.3) of 0.30N $NaHCO_3$ per kilogram body weight per hour were used. Animals were autopsied at periods ranging from four to eleven days.

RESULTS (See Fig. 1)

Series I. Instillation of Isotonic 0.10N HCl–0.2 Per Cent Pepsin Per Gastrostomy.—All five animals in this series developed duodenal ulcers in the posterior wall of the first portion of the duodenum (see Fig. 2). Variable degrees of duodenitis and gastritis were present. All of these animals developed an acidosis as was marked by vomiting, weakness, coma, and a drop in blood pH, which varied between pH 7.09 and 7.24 (average 7.15) immediately before sacrificing the animals.

Series II. Instillation of 0.10N HCl–0.2 Per Cent Pepsin Per Gastrostomy Plus 0.16N $NaHCO_3$ by Vein.—Fourteen dogs were used in this series. Daily blood pH determinations revealed that none of the animals developed acidosis or alkalosis. Blood pH values in these dogs ranged from 7.30 to 7.44 with an average value of 7.36. No case of gastroduodenal ulceration occurred. One animal which had received the acid pepsin solution for ten days developed a duodenal erosion which was proved microscopically. Variable degrees of gastritis and duodenitis were present. A number of animals developed vomiting, hematemesis and melena.

Series III. Instillation of 0.15N HCl—0.2 Per Cent Pepsin Per Gastrostomy Plus 0.30N $NaHCO_3$ by Vein.—Fourteen dogs were used in this series. None of the animals developed any change in blood pH as determined by daily

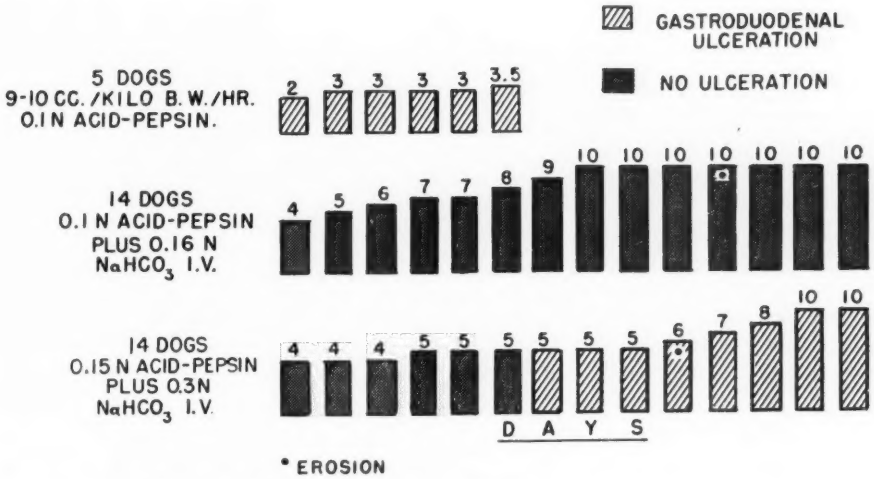

Fig. 1.—The effect of continuous intragastric infusion of acid-pepsin on the gastroduodenal mucosa of dogs.

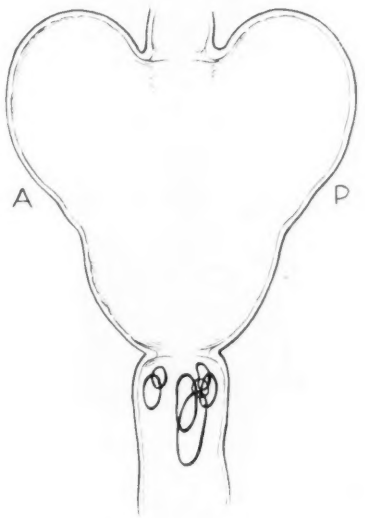

Fig. 2.

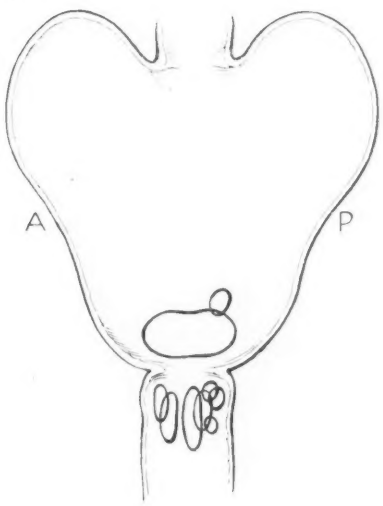

Fig. 3.

Fig. 2.—Diagram showing location and relative size of ulcers occurring in the five dogs which received 0.10N HCL-0.2 per cent pepsin intragastrically. Several animals had multiple ulcers. *A* indicates the anterior and *P* the posterior wall.

Fig. 3.—Diagram showing location and relative size of ulcers occurring in seven of the fourteen animals which received 0.15N HCL-0.2 per cent pepsin intragastrically and 0.30N $NaHCO_3$ intravenously. Several animals had multiple ulcers.

readings. Blood pH values in these dogs ranged from 7.32 to 7.43 with an average of 7.37. Seven of the fourteen animals developed either gastric or duodenal ulcerations (see Figs. 3 and 4). Variable degrees of melena, hematemesis, and vomiting were present. Duodenitis and gastritis were invariably present.

Fig. 4.—Photograph shows three ulcers located in first portion of duodenum of a dog in which 0.15N HCl and pepsin were continuously administered for eight days with blood pH maintained at normality by intravenous infusion with 0.30N $NaHCO_3$.

DISCUSSION

This study represents in part a confirmation of the work of Cummins, Grossman, and Ivy[1] who demonstrated that the acidosis which results from the intragastric infusion of acid plays a role in its injurious action on the gastroduodenal mucosa. In addition to confirming this finding, two additional facts emerge from the present study. First, the addition of pepsin to 0.10N HCl does not increase its ulcerogenic action under the conditions of our experiments. Second,

when blood pH is maintained at a normal value, 0.10N HCl-pepsin is not ulcerogenic whereas 0.15N HCl-pepsin definitely is ulcerogenic.

In evaluating the results of these experiments it must be borne in mind that we have used acid-pepsin mixtures and not natural gastric juice. In addition to acid and pepsin, other factors, either protective or destructive, may be present in gastric juice. For example, Meyer and his associates[2] have recently suggested that the lysozyme in gastric juice may be concerned in its ulcerogenic action.

In the introduction to this paper three questions were put forth. These questions are now presented again and an attempt is made to indicate what the present study reveals regarding their answers.

Can acid-pepsin alone in physiologic amounts and concentrations produce ulceration of the gastroduodenal mucosa? The theoretical maximum concentration of HCl which could be present in canine gastric juice is about 0.16N.[3] Hanson, Grossman, and Ivy[4] determined the average maximal secretory response to histamine in the dog and found it to be 8 c.c. per kilogram per hour of 0.14N HCl. In the present study it has been clearly shown that the introduction of acid-pepsin into the stomach at this rate and concentration leads to ulceration if it is maintained for six or more days. *Therefore, we may conclude that if the maximal secretory capacity of the stomach is maintained for six days or longer ulceration may be expected to occur.*

The next question that arises is, Is it possible to maintain secretion at this maximal rate for from five to ten days? In another study Hanson, Grossman, and Ivy[5] found that in dogs receiving supramaximal doses of histamine continuously, intravenously, or subcutaneously over periods of two to sixteen days, samples taken at various periods showed that the average acid concentration was about 0.125N and the average volume was about 40 c.c. per hour or approximately 4 c.c. per kilogram per hour. These dogs receiving histamine in this fashion all developed gastroduodenal ulceration. In other words, ulceration developed in spite of the fact that the rate of acid secretion falls considerably from the original maximal level. The present study does not permit us to draw a definitive conclusion on the question of whether the degree of hypersecretion observed in these animals receiving histamine continuously is sufficient to account for the ulceration that occurs. We need further observations on the amount and concentration of acid secreted by dogs receiving histamine continuously as well as further studies on the exact volume and concentration of acid which must be infused into the stomach to produce ulcer. In the present study, we have succeeded in mapping out the boundaries in a broad way.

How long must the gastroduodenal mucosa be exposed to what concentration of acid-pepsin in order for ulceration to result? The action of injurious agents on living cells reveals a characteristic relationship between the strength of the injurious agent and the length of time during which it must act to produce injury. When such a relationship is plotted graphically a curve which is called a strength-duration curve is obtained. So far we have determined only one point on this curve, namely, that 0.15N acid-pepsin must act for six days or longer to produce ulceration, when 8 c.c. per kilogram per hour is used. Furthermore, we know that with this volume the threshold of acid concentration required

for ulceration within ten days is between 0.10N and 0.15N. It is reasonable to assume that the 0.10N acid-pepsin might lead to ulceration if it were permitted to act long enough, particularly in view of the fact that gastritis, duodenitis, and melena occurred with this concentration of acid. We are continuing studies in which the concentration and the volume of acid are being varied separately to determine further points on the strength-duration curve.

To what extent does pepsin enhance the injurious action of acid gastric juice? Schiffrin and Warren[6] perfused jejunal loops with 0.10N HCl solution for twelve hours and observed only superficial damage to the villi. When pepsin was added to the acid solution, ulceration and perforation occurred. It is clear from this and from other similar studies that pepsin definitely increases the injurious action of acid solutions. Driver[7] in similar perfusion experiments showed that the ulcerogenic action was not increased by using a high instead of a low concentration of pepsin. Schiffrin and Warren[6] also demonstrated that when acid was perfused through the stomach into the duodenum it picked up pepsin and that the addition of pepsin to the perfusing fluid did not enhance its ulcerogenic action.

In the experiments of Cummins, Grossman, and Ivy,[1] intragastric infusion with 0.10N HCl for periods as long as twelve days did not lead to ulcer formation provided blood pH was maintained at a normal level. In the present studies the addition of pepsin to 0.10N HCl failed to produce ulcers in periods of observation extending up to ten days.

Furthermore, in the present studies 0.10N HCl-pepsin did not produce ulceration whereas 0.15N HCl-pepsin did. The 0.10N HCl-pepsin solution has a pH of about 1.1 whereas the 0.15N HCl-pepsin solution has a pH of about 0.89. Pepsin does not show an increase in proteolytic activity as the pH is lowered below 1.0 and in the case of some protein substrates there is actually a decrease.[8] This means that the peptic activity of the 0.10N HCl-pepsin solution can be considered to be the same as that of the 0.15N HCl-pepsin solution. Therefore, the fact that the former is not and the latter is ulcerogenic must be ascribed to the difference in acidity of the two solutions and not to the difference in peptic activity. This is contrary to the theory of Le Veen[9] that the ulcerative action of acid-pepsin solutions is mainly dependent upon their peptic activity.

It is possible that sufficient pepsin is present in the stomach so that 0.15N HCl alone without pepsin would produce ulcers just as readily as the 0.15N HCl-pepsin mixture.

SUMMARY

1. Five dogs receiving 9 to 10 c.c. for each kilogram of body weight each hour of 0.10N HCl–0.2 per cent pepsin through a gastrostomy developed duodenal ulcers in from forty-eight to eighty-four hours. These animals also developed an acidosis as was evidenced by a drop in blood pH. Duodenitis and gastritis were invariably present.

2. Fourteen dogs receiving a similar amount of acid-pepsin solution through a gastrostomy were simultaneously given 0.16N $NaHCO_3$ intravenously to prevent acidosis. None of these animals developed gastroduodenal ulcers, even if

acid-pepsin was continuously administered for ten days. Variable degrees of gastritis and duodenitis were present.

3. Fourteen dogs were continuously subjected to intragastric administration of 0.15N HCl containing 0.2 per cent pepsin through a gastrostomy and intravenous infusion of 0.30N $NaHCO_3$ to prevent acidosis. Seven animals surviving five days or more developed gastric or duodenal ulcers. Gastritis and duodenitis were invariably present.

CONCLUSIONS

1. The acidosis which accompanies intragastric administration of acid is an important factor in the development of gastroduodenal ulcer. Prevention of the acidosis prevents ulcer formation when 0.10N HCl (with or without pepsin) is infused into the stomachs of dogs.

2. The threshold of acid concentration needed to produce ulceration lies between 0.10N and 0.15N when 8 to 10 c.c. per kilogram body weight per hour are infused continuously into the stomachs of dogs for six days or longer and the blood pH is kept normal.

3. The present studies do not permit a conclusion to be drawn concerning the role of pepsin in the production of these ulcers.

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A NEW METHOD FOR THE ROENTGENOLOGIC STUDY OF THE RECTUM

GEORGE LEVENE, M.D., BOSTON, MASS.

(From the Department of Radiology, Massachusetts Memorial Hospitals, and Boston University School of Medicine)

ROENTGENOLOGIC study of the rectum is commonly regarded as having little value. Some believe it is definitely misleading. Jones[1] advised against its use and stated that the average roentgenologist can make a correct diagnosis in only 40 per cent of the cases. He felt that "the correct diagnosis in many clinics in carcinoma of the rectum is so low that x-ray should not be used." Feldman[2] said, "In the early periods when the condition is in its incipiency the diagnosis is often difficult and in such instances the x-ray diagnosis may be misleading." The personal experience of many roentgenologists and surgeons leads them to accept these statements without dispute. Analysis of the problem shows that unsatisfactory examination by the usual roentgenologic methods is due to three factors: (1) indifference on the part of the roentgenologist because the rectum is readily accessible to other methods of examination; (2) the superimposition of barium-filled segments of rectum and sigmoid; (3) the lesion is frequently hidden by the mass of barium introduced into the bowel.

Since all lesions of the alimentary tract arise in the walls, it seemed desirable to study the walls by coating them with an opaque substance to render them visible. Obviously, such a method would not have the disadvantage of the customary procedure of filling the rectum with an opaque suspension which hides the lesion one is attempting to find. Satisfactory visualization of the mucosa was achieved by spraying the lower segment of the intestine with a thin suspension of barium sulfate in water. Numerous technical difficulties were encountered in developing a suitable technique. Spraying equipment usually requires compressed air for its operation. It must be remembered, however, that the alimentary tract is vulnerable to a sudden increase of pressure, the average bursting pressure for the entire tract being 4.07 pounds.[3] Such pressure can be reached in a few seconds with ordinary paint-spraying equipment. The problem of spraying without building up internal pressure was solved by the development of new equipment.

APPARATUS

The apparatus (Fig. 1) consists of a metal tip, ½ inch long and ¼ inch in diameter. The tip has a central orifice, $\frac{1}{100}$ inch in diameter, through which a mist of barium suspension is propelled. Communicating with this orifice are two ducts, one of which is connected by a catheter to a syringe containing 10

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c.c. of barium suspension, and the other to a reduction valve attached to a tank of oxygen. The reduction valve is set at 2 pounds. The metal tip is further provided with two relatively large orifices which permit the compressed gas, which is introduced into the bowel in spraying, to escape back through a tube out of the bowel. No gas can therefore accumulate to build up pressure in the body cavity. The cross-sectional area of the escape vents is 200 times the area of the spraying orifice. A large safety factor is thus provided to insure an adequate avenue of escape for any gas introduced into the bowel. The catheters are surrounded by a helical spring and the entire assembly is encased in soft rubber tubing. The tubing provides the channel of exit for the gas. The purpose of the spring is to prevent the anal sphincter from compressing the rubber tubing. A patent exhaust vent is thus assured.

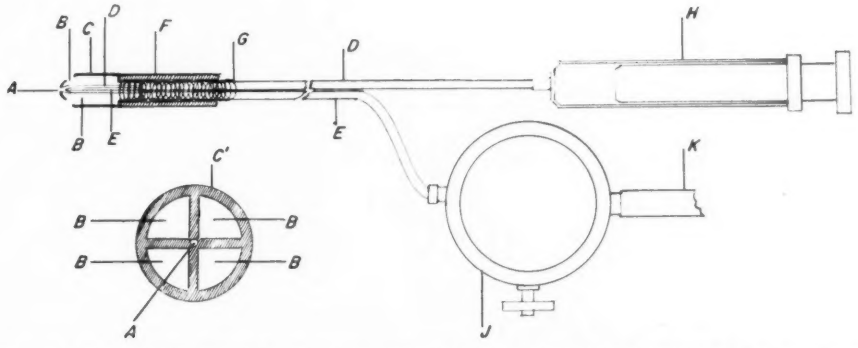

Fig. 1.—Schematic drawing of spray assembly. *A*, Spraying orifice; *B*, air return vents; *C*, wall of spraying tip; *D*, duct for barium suspension connected to syringe; *E*, duct for compressed air or oxygen connected to reducing valve; *F*, wall of rubber tubing; *G*, helical spring; *H*, syringe containing barium sulfate suspension; *J*, reducing valve; *K*, hose connection to oxygen tank.

METHOD

The bowel must be thoroughly clean for examination. The patient is placed in a knee-shoulder position on the fluoroscopic table and, with the gas flowing through the apparatus, the tube is inserted into the bowel until the tip is well up in the sigmoid. The steady current of gas insures patency of the spraying orifice and gently separates the walls of the gut, making the surfaces accessible to the spray. The position of the tip is checked on the fluoroscopic screen. The patient is then placed in a prone position with the head of the table lowered. Gas introduced into the bowel will thus rise to the distal segment of the gut and find its way out through the escape orifices of the spraying tip and the rubber tubing. The gas pressure introduced into the bowel by this procedure is 0.6 ounce, which is approximately $\frac{1}{100}$ of the average bursting pressure. Barium is then forced out of the syringe while the spraying tip is slowly withdrawn. A fine mist of barium sulfate suspension is thus deposited on the mucosa, from above downward. Spraying is continued until the tip presents externally. In this manner the anal canal is also visualized. Stereoscopic films in the anteroposterior, posteroanterior, and lateral positions are then taken.

ANATOMIC CONSIDERATIONS

The rectum begins at its junction with the sigmoid at the level of the third sacral vertebra and ends at the pelvic diaphragm where it joins the anal canal. It is usually 12.5 to 15 cm. in length and has the largest caliber of any portion of the colon. When seen from the side, it has two convexities, an upper anterior and a lower posterior curve. From the front, the borders appear bilaterally convex, and are interrupted by lateral inflections of the walls, the largest

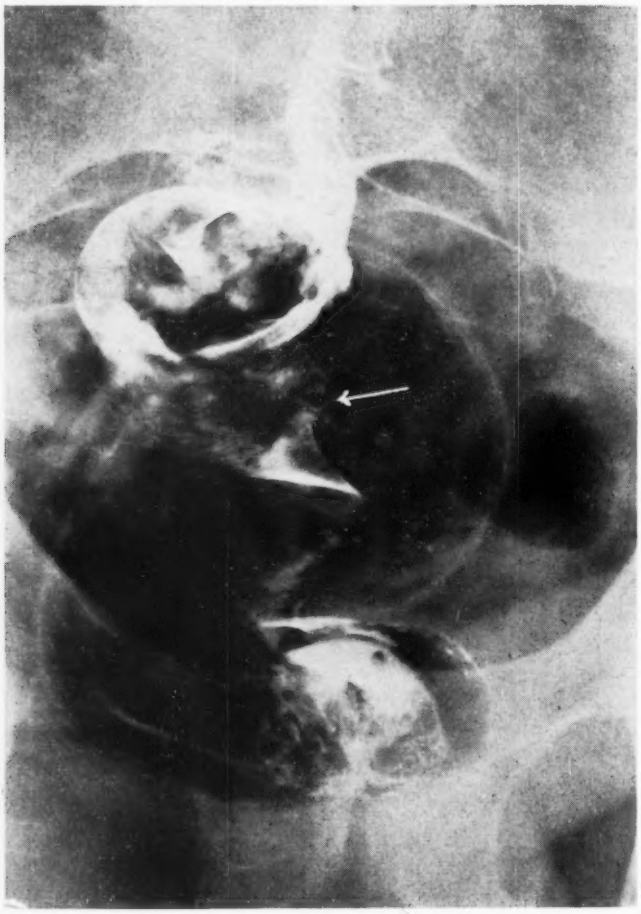

Fig. 2.—Chronic proctitis. Houston's valves are indurated and project into the lumen as rigid structures. A small area of ulceration is shown on the superior surface of the upper valve (arrow).

of these being opposite the lowest valve of Houston. This marks the point of reflection of the peritoneum. The rectal mucosa is smooth, but presents three semilunar folds in which are contained circular muscle fibers and a supporting stroma. These are the valves of Houston. There are usually two on the left and one on the right, the latter at a point midway between the left valves. At rest, these structures are normally approximated so that they form an effectual seal, dividing the rectum into an upper and lower ampulla. Functionally, the

upper ampula is a reservoir, while the lower ampulla serves merely as a passageway. During defecation the valves are retracted so that the rectum becomes one continuous tube. The valves play an important role not only in normal physiologic processes, but they are frequently the seat of important pathologic changes which may easily be overlooked on proctoscopic examination. Distally, the rectal mucosa is gathered into vertical folds, the columns of Morgagni. Little pockets are thus formed between the folds which are known as the crypts of Morgagni. The crypts and lower ends of the columns are covered by a continuous, serrated ring of tissue called the anal papillae. Immediately below this point, the rectal mucosa is lighter in color due to the underlying fibers of the internal sphincter muscle. This zone is known as the anorectal line, or "white line of Hilton."

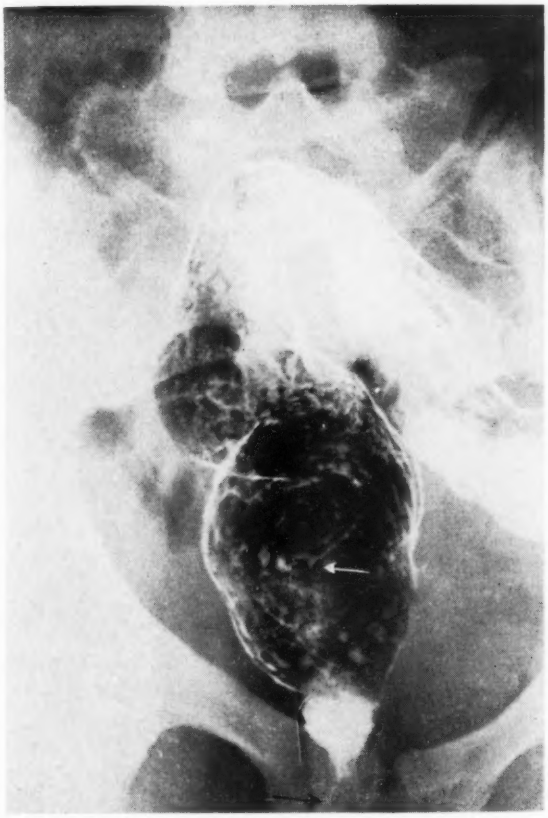

Fig. 3.—Chronic ulcerative colitis. The rectum is contracted. The mucosa is granular and only a faint remnant of one of Houston's valves remains (upper arrow). The anal fistula (not well reproduced on print) is shown by the lower arrow.

The anal canal begins at the pelvic diaphragm and ends at the anus. Its length varies from 3 to 5 cm. Normally, on roentgenologic examination, it presents two or three delicate, closely approximated vertical folds.

The advantage of the spray technique over ordinary roentgenologic methods in demonstrating normal and pathologic conditions of the rectum is shown in the following case reports.

CASE REPORTS

CASE 1.—Chronic proctitis. Mr. C. G., aged 39 years, had a complaint of constipation. X-ray examination with spray technique (Fig. 2) showed that the rectal mucosa was indurated. Houston's valves were rigid and protruded into the lumen. There was a small area of ulceration on the superior surface of the upper valve. The mucosa of the lower ampulla was ulcerated, the folds of the columns of Morgagni being almost completely destroyed. These findings were confirmed by proctoscopy.

CASE 2.—Chronic ulcerative colitis. Mrs. C. B. G., aged 26 years, complained of blood and small amounts of pus per rectum. X-ray examination with spray technique (Fig. 3) showed the rectum to be contracted. There was marked induration of the entire rectal mucosa which appeared coarsely granular. Houston's valves were shrunken and rigid. Similar changes were noted in the anal canal. There was a small fistulous tract extending laterally from the right wall of the canal. The findings were confirmed by proctoscopy.

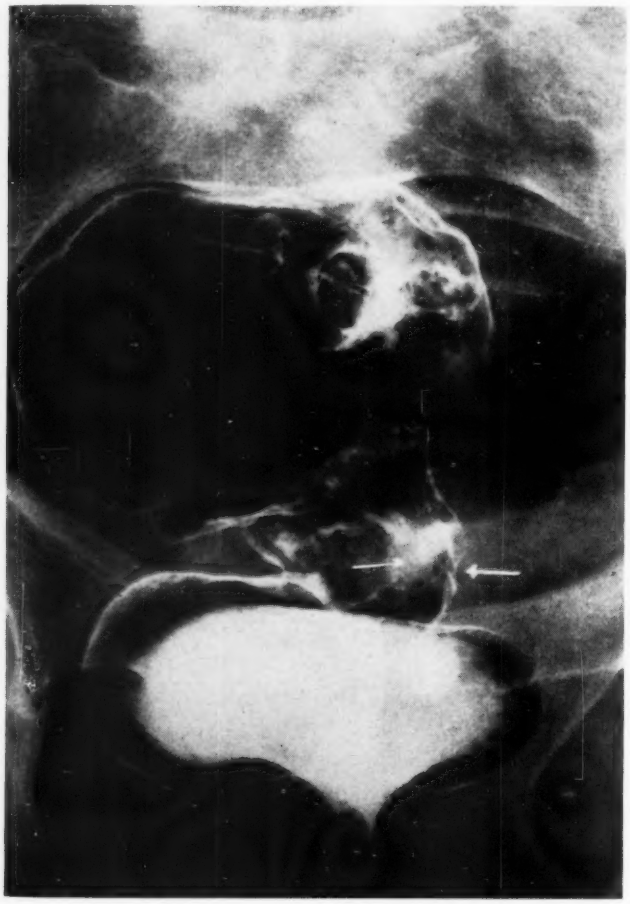

Fig. 4.—Carcinoma of the rectum, annular type. The stenosed upper rectal ampulla is indicated by arrows.

CASE 3.—Carcinoma of the rectum. Mr. M. S., aged 67 years, had rectal discomfort accentuated on defecation for the past four months and bright red rectal bleeding for the past two months. X-ray examination with spray technique (Fig. 4) showed a marked degree of stenosis of the upper rectal ampulla. The lumen was reduced to the caliber of a pencil by an annular neoplasm. The involved segment was slightly prolapsed into the lower rectal ampulla. These findings were confirmed by proctoscopy and operation.

CASE 4.—Carcinoma of the rectum. Mr. E. J. S., aged 43 years, had a complaint of increasing constipation for three months, bleeding, and slight pain on going to stool. A routine barium enema showed a normal appearance of the colon and rectum. Examination with the spray technique (Fig. 5) revealed an irregular filling defect of the anterior wall of the lower rectal ampulla corresponding to a cauliflower mass involving approximately three-fifths of the circumference of the rectum. This was confirmed at autopsy.

Fig. 5.—Roentgenogram made after spray examination. Carcinoma of the rectum—cauliflower mass. The edges of the mass are indicated by white arrows. The uninvolved posterior wall, outlined by gas, is indicated by black arrows. Anteroposterior and lateral films taken after routine barium enema failed to reveal any filling defect of the rectum.

CASE 5.—Sessile polyp of the rectum. Mr. M. J., aged 65 years, complained of bleeding from the rectum. A routine barium enema showed a normal appearance of the rectum. X-ray examination with spray technique (Fig. 6) showed a small sessile polyp measuring 4 by 10 mm. attached to the left lateral wall of the rectum at the level of the peritoneal reflection. This was confirmed by proctoscopy and operation.

COMMENT

In agreement with other observers, my experience has shown the inadequacy of routine barium enema for the detection of rectal pathology. Even large tumors are often obscured by barium. The air contrast enema is also disappointing because it is frequently difficult to distinguish between air bubbles and organic filling defects. Moreover, the procedure is usually uncomfortable for the patient. A "negative" report on examination with a barium enema does not necessarily indicate the absence of disease. The fact that the rectum can be

examined digitally or proctoscopically does not obviate the need for refinement of roentgenologic study, for these methods, too, may have their limitations. Hirschman[4] stated that the valves of Houston "are of considerable importance because of the fact that when they are infiltrated, thickened or enlarged, they offer an obstruction to the fecal current and stercoral ulcerations concealed on their upper surfaces are often overlooked, whose discovery would clear up the etiology of some cases of chronic diarrhea."

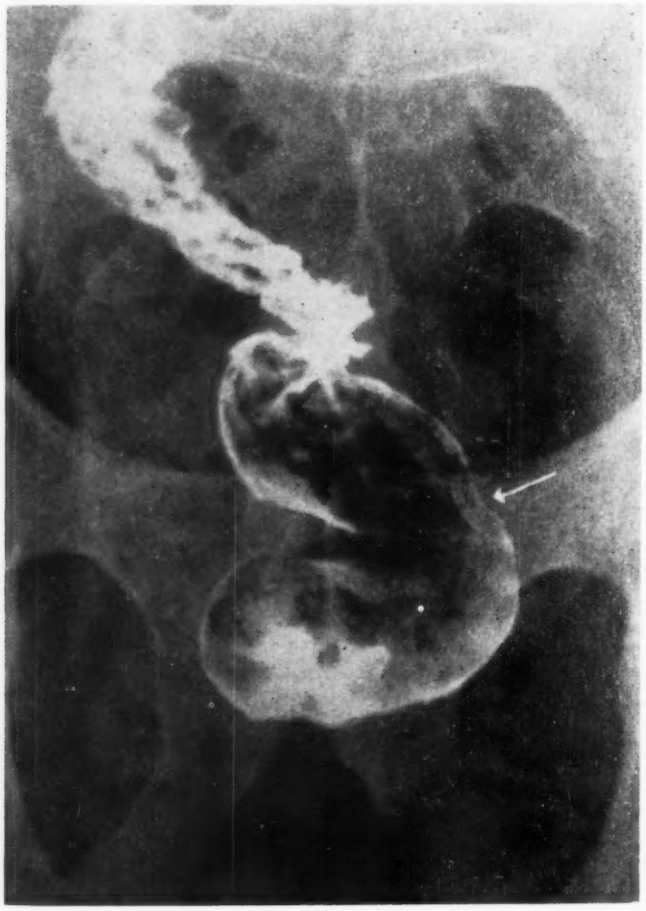

Fig. 6.—Roentgenogram made after spray examination. A sessile polyp is shown by the arrow. This polyp could not be shown by routine barium enema.

The method of examination here described has been used in the study of 100 patients. In every case, examination by the spray technique was followed by routine barium enema, and in some cases, also, by air contrast enema. Opportunity was thus afforded not only to compare the value of these different methods of examination but to compare the reactions of the patients to these different procedures. In no case was there any discomfort or untoward effect with the spray technique.

Examination by the spray technique appears to possess the advantage of visualizing the rectal mucosa and its structures in their physiologic state. In the routine barium enema such structures as Houston's valves and the columns and crypts of Morgagni are rarely demonstrated, being either obscured by the mass of opaque barium introduced into the bowel or flattened out by the mass of barium so that they can no longer be identified. There is no significant distention of the rectum with the spray technique, so that the smaller anatomic structures are, as a rule, clearly visualized.

Limitations of space do not permit a more detailed presentation of the anatomy and physiology of the rectum as shown by the spray technique. These are discussed elsewhere.[5]

SUMMARY AND CONCLUSIONS

A new method for the roentgenologic study of the rectum is described. It consists of spraying a thin mist of barium sulfate suspension on the rectal mucosa. This technique is made possible by the development of new apparatus which allows spraying without building up internal pressure. The procedure is safe and is attended by no discomfort. This method of examination has revealed lesions of various types which were not demonstrated by routine barium enema.

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INTUSSUSCEPTION DUE TO HETEROTOPIC PANCREAS

Report of a Case

Charles B. Ripstein, M.D., Montreal, Canada

(From the Department of Surgery, Royal Victoria Hospital)

HETEROTOPIC pancreatic tissue occurs fairly commonly in the gastrointestinal tract. In a recent review, Barbosa and associates[1] stated that approximately 470 cases have been recorded in the literature. Duff, Foster, and Bryan,[5] analyzing the material from the Department of Pathology at McGill University, reported an incidence of slightly over 1 per cent in routine autopsies.

Aberrant pancreatic rests may be located almost anywhere within the abdominal cavity. The frequency with which specific organs are involved varies in different reports., but on the average the duodenum is the most common location, stomach jejunum and ileum are next, while the gall bladder, spleen, mesentery, and omentum are rarer sites.

Clinical symptoms due to aberrant pancreatic tissue are said to occur in at least 50 per cent of the cases. The type of syndrome produced varies with the location of the rest.

It seems logical that a pancreatic rest in the small bowel would frequently cause intussusception, but apparently such a phenomenon has rarely been observed. Bosworth and Stein[3] have recently reported a case of intussusception due to aberrant pancreas, and they stated that only three previous cases have been recorded in the literature, by Eliot and Corscaden,[6] Benjamin,[2] and Steiger.[7] The present case constitutes the fifth report.

CASE REPORT

S. P., a girl aged 17 years, was admitted to the Royal Victoria Hospital, March 1, 1947. She gave a history of recurrent attacks of colicy lower abdominal pain since childhood. These attacks were characterized by a sudden onset of severe pain accompanied by nausea and some abdominal distention. She had never noticed blood in the stool and apart from the episodes of pain had no complaints. The last attack had occurred six hours before admission. On examination the patient was a well-nourished, well-developed young girl, not acutely ill. The abdomen was slightly distended but there were no areas of tenderness or muscular rigidity and no mass could be felt. Physical findings were essentially negative. Investigation, by barium enema, revealed no abnormalities in the bowel. Intravenous pyelogram showed a normal genitourinary tract. Gynecologic consultation confirmed the fact that the pelvis was normal.

On March 5 she experienced another attack of colicy abdominal pain below the umbilicus, and exploratory laparotomy was performed.

Under spinal anesthesia, the abdomen was opened by a right transverse incision. An ileo-ileal intussusception was found with no evidence of strangulation. This was easily reduced and the apex of the intussuscipiens was seen to be a walnut-sized reddish-gray tumor in the antimesenteric wall of the ileum, twelve inches from the ileocecal valve. This was resected with a wedge of bowel, and continuity was re-established by a two-layer end-to-end anastomosis.

The postoperative course was uneventful and the patient has had no further attacks of abdominal pain.

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*Pathologic Report** (Fig. 1).—The specimen consisted of a round, hard encapsulated mass 2½ cm. in diameter. It had a reddish-gray surface. The cut section showed a mass of finely lobulated yellow tissue which was well encapsulated and interlaced by fibrous bands.

Sections of the tumor showed flattened and eroded small bowel mucosa over the surface. The tumor itself was seen to consist of normal-appearing pancreatic tissue arranged in the usual alveolar fashion with numerous islets present. There was no evidence of malignancy.

Diagnosis was heterotopic pancreatic tissue in ileum.

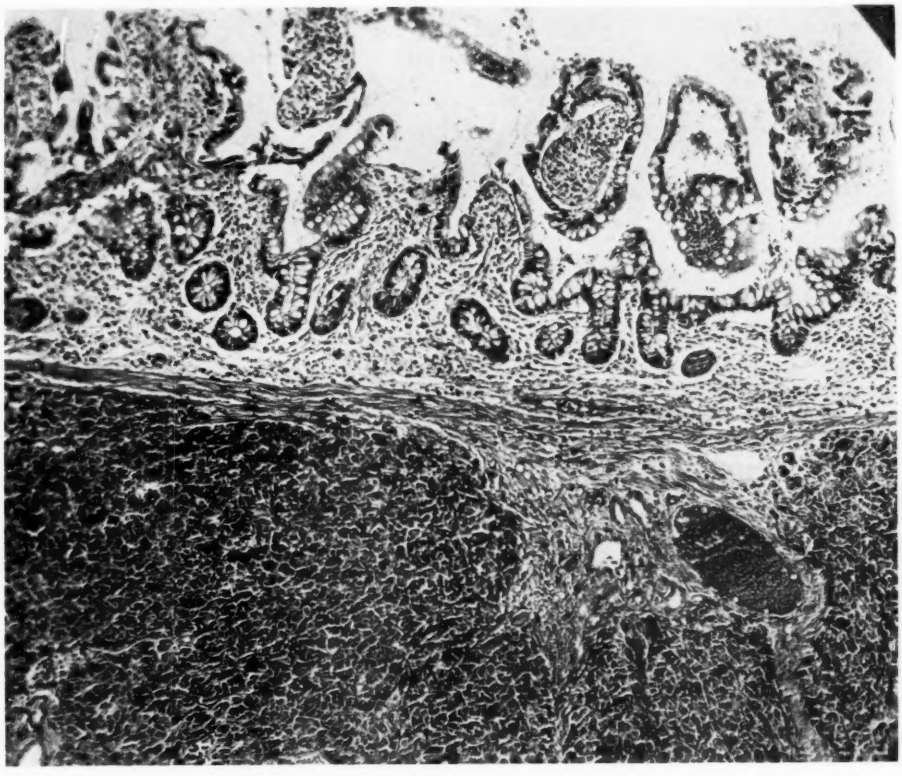

Fig. 1.—Photomicrograph of specimen showing heterotopic pancreatic tissue in the submucous layer of the ileum.

SUMMARY

A case of intussusception due to aberrant pancreatic tissue in the ileum is reported.

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*Dr. T. R. Waugh.

DIVERTICULA OF THE VERMIFORM APPENDIX

ANDREA SACCONE, M.D., VITO W. A. DILLUVIO, M.D., AND
EUGENE I. ZINS, M.D., NEW YORK, N. Y.

(From the Department of Pathology of the Metropolitan Hospital)

THE incidence of inflammation and perforation of diverticula of the appendix is much greater than the incidence of inflammaton and perforation of the appendix itself.[1] The obvious inference is that should such a diverticulum be encountered in the course of a surgical procedure, appendectomy is definitely indicated. To the pathologist this condition is of interest in relation to its incidence, classification, and pathogenesis.

Two types of diverticula have been described, the false type and the true type. False diverticula are generally considered to be those which contain mucosa, submucosa, and serosa but lack the muscularis. A true diverticulum contains all the muscle layers and is, in truth, a reduplication of the vermiform appendix extending from a parent appendix. There is a distinction between a congenital true and an acquired true diverticulum. The former cannot be distinguished from a normal appendix containing a thick muscular layer. The latter is also a true diverticulum since all three layers of the appendical wall, although atrophic, are present.[2]

Concerning pathogenesis, the false diverticulum is usually the result of inflammation of the appendix. It appears at weak spots in the wall and can be described as a mucosal hernia. Inflammation is not involved in the genesis of the true diverticulum. True congenital diverticula are pathologic rarities and develop during the growth of the fetus.[3] True acquired diverticula are considered to be caused by intrinsic or extrinsic pressure. The etiopathogenic theories at best are inconclusive. Embryologic, mechanical, and reflex factors have been considered but, due to the rarity of the condition, opportunities for study have been few.

A congenital diverticulum was reported in a full-term stillbirth by Hedinger.[4] Bachlechner[5] reported an example of a large twisted appendical diverticulum occurring at the base of the appendix in a 17-year-old boy. Others reporting instances of true diverticula include Mertens,[6] Sturm,[7] Schmincke,[8] Malone[9] and Altemeier.[10] According to Kline, Young, and Strauss,[1] some diverticula reported as instances of the true variety were quite possibly false, observed long after the original inflammation had completely subsided.

Distinction between true congenital and true acquired diverticula has been made only rarely in the literature. Our case is an instance of true acquired diverticulum. It is presented with the dual purpose of focusing attention on the fact that such diverticula do exist and of clarifying the classification of these infrequently described lesions.

Received for publication, April 8, 1948.

REPORT OF CASE

J. C., a white man aged 58 years, was admitted to the Columbus Hospital, New York, N. Y., on Dec. 15, 1946, because of right inguinal hernia and vague pain in the right lower quadrant of the abdomen. The hernia had been present for many years and was associated with discomofrt and several recurrent attacks of pain in the right lower abdomen.

The significant physical findings were an easily reducible large mass in the right inguinal region and a soft, nondistended, nontender abdomen.

Urinalysis was reported normal. The blood count showed hemoglobin of 90 per cent, erythrocytes 4,790,000, leucocytes 10,800 with 74 per cent mature polymorphonuclears, 2 per cent band forms, 20 per cent lymphocytes, and 6 per cent monocytes.

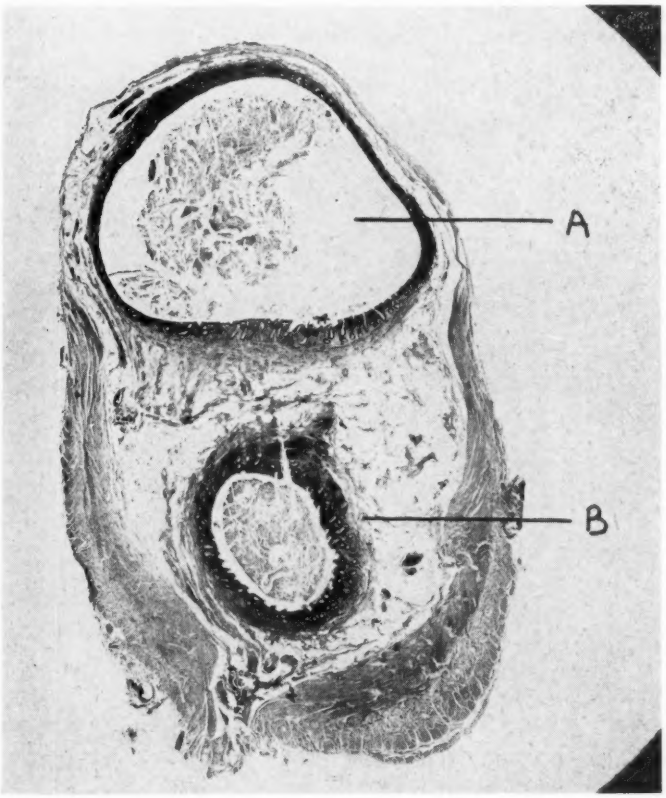

Fig. 1.—A, Diverticulum; B, appendix. (Low power, magnification ×9.)

A diagnosis of right inguinal hernia and subacute appendicitis was made on the basis of history and physical findings. An appendectomy and a right inguinal hernioplasty were performed. The patient had an uneventful and rapid postoperative recovery.

Gross Description.—The appendix was 6 cm. in length, 0.5 cm. in diameter, and presented two small lateral bulgings in its mid-portion. The small masses measured 0.5 cm. in length and they were closely apposed but independent of one another, being separated by a very thin band of tissue. The appendix showed only slight congestion of the serosa and mucosa. The small masses at the middle of the appendix proved to be saccular evaginations of the appendix, communicating with the parent organ by way of very narrow stomas.

Microscopic Examination.—The small saccular masses disclosed all the layers of normal appendix. Each was formed of serosa, very thin muscularis, submucosa, and mucosa.

Beneath the mucosa were areas of lymphoid tissue. There was no evidence of present or past inflammation. The histology of the diverticulum was indistinguishable from that of the normal appendix despite the thinness of the walls of the saccular masses.

COMMENT

By establishing a definite classification including false diverticula, true congenital and true acquired diverticula, in the future light may be shed on the pathogenesis of these lesions. True diverticula have been reported haphazardly in the past, including any lesion containing all three layers of the appendix. Inference has been made that all such lesions are congenital. There does not seem to be any rational embryologic explanation for the occurrence of such a lesion. Nevertheless, the possibility of occurrence is not disputed but careful

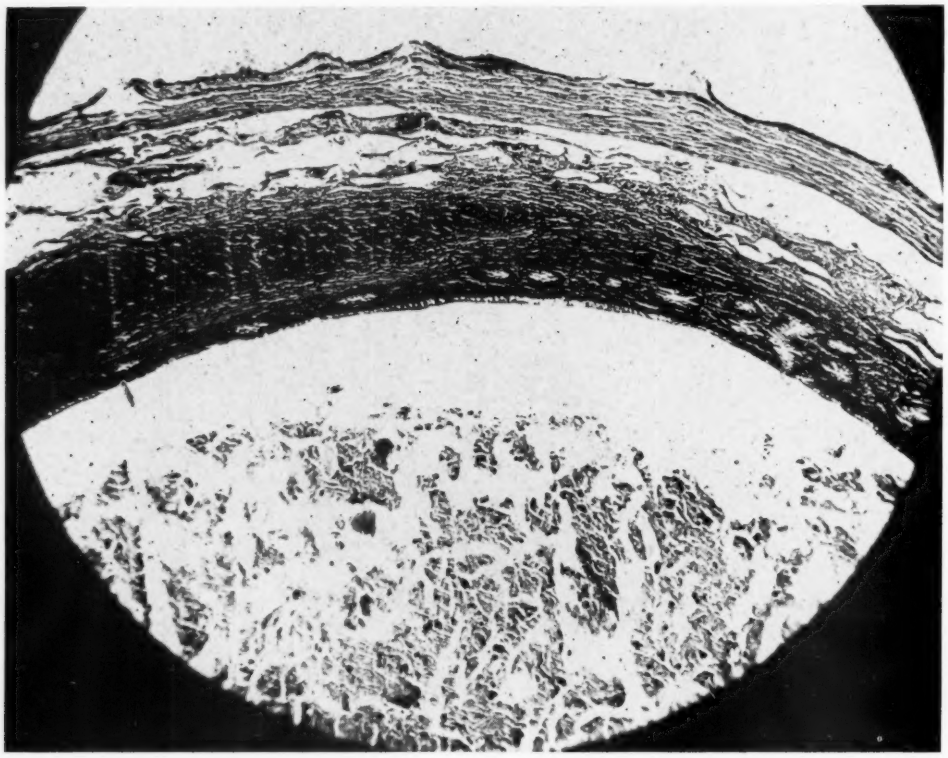

Fig. 2.—Wall of diverticulum with mucosa, submucosa, muscularis, and serosa. (High power, ×50.)

consideration is urged of all diverticula of the appendix. Acquired lesions are true diverticula in the sense that the muscularis is present. The atrophy of this layer bespeaks a pulsion or traction origin of the lesion. Our example is typical in that all the layers of the appendix are present. The muscularis surrounding the appendix is evidently atrophic. Reclassification of true diverticula will undoubtedly place the majority in the true acquired group.

CONCLUSION

1. A more definitive classification for diverticula of the appendix is presented.

2. Differentiation between types of diverticula of the appendix is made on a basis of pathogenesis and histopathology.

3. An example of true acquired diverticulum of the appendix is reported.

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MELANO-EPITHELIOMA OF THE ANUS AND RECTUM

Report of Cases and Review of Literature

Frederick W. Braastad, M.D.,* Malcolm B. Dockerty, M.D.,†
and Claude F. Dixon, M.D.,‡ Rochester, Minn.

MELANO-EPITHELIOMA of the anus and rectum comprises approximately 0.25 per cent of anorectal malignant neoplasms of all types and about 1 per cent of all epitheliomatous lesions of this location. Its superficial position affords opportunity for early diagnosis, but for the same reason, spread by the lymphatics and blood vessels of both portal and peripheral systems is also manifest at an early date. Few men have had the privilege of studying large series of these neoplasms; therefore, when we recently encountered a 61-year-old veterinarian who had an anal melano-epithelioma (Case 10, Tables I and IV[1-7]) we decided to review the subject and to report the experiences at the Mayo Clinic with a group of ten patients who suffered from the effects of this type of tumor.

HISTORICAL DATA

Laennec, in 1806, first gave a good description of melanotic tumors as they affect man. For several years prior to this time veterinarians had described hereditary "black tumors" of the rectum of white and gray horses. It was not until 1857, however, that Moore first described a case of melanoma of the rectum of man. Virchow, in his "Pathology of Tumors" in 1869, quoted the report of the case of Maier and reported that he himself had encountered a case in which the disease ran a very malignant course. In 1883 Paneth[8] gave a complete account of his own case in addition to a résumé of the eight cases reported up to that time. In 1888 Schmidt-Petersen, in his inaugural thesis at Kiel, reported on nineteen cases, of which one was his own. In the same year Tuffier, in the *Archives Generales de Medecine*, commented on the frequency with which these tumors were pedunculated.

There followed the theses of several German authors, the most important of which was that of Sigerist in 1898, who reviewed 20 cases. At that time in France, Quénu and Hartman, in "Surgery of the Rectum," gave a description of these lesions which likewise was based on a study of about 20 cases. In 1901 Heller[9] reviewed the data on 25 cases, and the thesis of Loques in Montpellier in 1908 included a description of 2 additional examples. In 1912 and 1913 Chalier and Bonnet published several papers that covered this subject in the greatest detail; they described each of the 63 cases reported up to that time and also reported a case of their own.

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*Fellow in Surgery, Mayo Foundation.
†Division of Surgical Pathology, Mayo Clinic.
‡Division of Surgery, Mayo Clinic.

TABLE I. DATA ON TEN CASES OF MELANO-EPITHELIOMA OF THE ANUS AND RECTUM ENCOUNTERED AT THE MAYO CLINIC

CASE	AGE (YEARS) SEX	SYMPTOMS, DURATION AND TYPE	LESION		OPERATION		FOLLOW-UP PERIOD (MONTHS), RESULTS
			SITE AND DESCRIPTION	PATHOLOGIC DIAGNOSIS	DATE	TYPE	
1	67 F	8 months: Sacral backache. 6 months: Frequency and urgency of defecation; blood in stool; prolapse of mass; painful defecation	From internal sphincter 3 inches up rectum; left wall; 2.5 cm. in diameter; diagnosis of degenerating anal polyp	Melano-epithelioma	10/ 2/21 10/ 4/21	Left inguinal colostomy; posterior excision of rectum and 2 inches of sigmoid	20; death "general metastasis"
2*	58 F	5 months: Fullness and pressure in rectum; frequent small stools	Left posterior anal wall; 3 by 5 cm., ulcerated, bleeding, indurated, no fixation	Melano-epithelioma, with glandular involvement	8/ 9/22	Posterior excision of 2.5 inches of anus and rectum	4.5; death
3†	44 M	3 weeks: Frequency and urgency of defecation with pain; bloodstreaked stools	Anterior anal wall; ulcerated, pigmentation of anterior anal skin	Melano-epithelioma	8/23/29	Local excision	20; death, "lung metastasis"
4	68 M	2 months: Rectal pain; pus and blood in stools; rectal lump felt by patient	Anterior anorectal region "6 cm. from rectum"; 3 by 5 cm., fixed	Melano-epithelioma	10/ 4/32	Local excision (Quénu-Tuttle)	4; death, "liver and omentum involved"
5†	39 M	4 years: Pain on defecation, blood on paper; frequent "pile treatment"	External and internal hemorrhoids; scarring of anal canal	Hemorrhoids, with associated early melano-epithelioma	12/29/33	Hemorrhoidectomy	100; living and well
6*	59 F	8 weeks: Constipation; blood in stools	From dentate margin upward 4 cm., anterior; fixed, polypoid, 4 by 3 cm.	Melano-epithelioma, with glandular involvement	4/ 6/37	Left inguinal colostomy; perineal resection of rectum	4; death, "liver and lung metastasis"
7*	62 M	3 months: Rectal pain; urgency of defecation; bleeding from rectum	Lower third of rectum; began just above dentate line, anterior and right; large, crateriform, fixed	Melano-epithelioma (biopsy)	7/ 5/37	Palliative loop colostomy (liver involved)	5; death, "widespread metastasis"
8*	52 F	No rectal symptoms; lesion removed in postoperative dressing section	Anal margin; "small polyp"	Melano-epithelioma	9/21/37	Local excision	100; living and well
9	63 M	4.5 years: Rectal pain and itch; nodule excised elsewhere from anal region in February, 1941; ulcers spread to involve left groin and pubis	Ulcerating lesions in pubis and left groin; grade 4 edema of left leg with thrombophlebitis; edema of penis and scrotum	Melano-epithelioma (diagnosed from slides sent in)	No operation or biopsy at clinic; patient seen in June, 1942		5 (from time seen at clinic); death, "abdominal metastasis"
10	61 M	5 months: Protruding anal mass; 12 pound weight loss. 2 months: Bleeding from rectum	Just above dentate margin; left anterior quadrant; firm, polypoid, submucosal infiltration, pigmented areas	Melano-epithelioma; 3 cm. in diameter	4/22/47 5/23/47	Single barrel colostomy; radical posterior resection of anus, rectum, rectosigmoid and sigmoid (35 cm.)	4.5; living and well

*Studied by Vickers.[1]
†Reported by Smith and Broders.[2]

INCIDENCE

Eighty-six cases of melanotic tumors of the anus and rectum have been reported in the literature up to the present writing. The first 64 of these, as just described, were included in the review made by Chalier and Bonnet[10]; the last 22 cases have been reported since that time, generally as individual case reports.[2, 5, 6, 7, 11-24]

Up until April, 1947, 10 patients with this condition have been seen at the Mayo Clinic, including our own case (Table I). Two of them have been reported previously[2] and are included in the 22 cases described since Chalier and Bonnet made their report; therefore we are actually adding 8 cases to the literature, making a total of 94 described to date.*

Sex.—The sex has been noted in 86 of the 94 reported cases; 55 patients were men and 31 were women, a ratio of 1.8:1.

Age.—Age has been noted in 84 instances. Seventy-six per cent of the patients were between the ages of 40 and 70 years (Table II). The youngest patient was 22 and the oldest was 78 years.

TABLE II. AGE DISTRIBUTION OF EIGHTY-FOUR PATIENTS

AGE (YEARS)	MEN	WOMEN	TOTAL
20-29	5	0	5
30-39	6	3	9
40-49	12	7	19
50-59	8	10	18
60-69	18	9	27
70-79	5	1	6

PATHOLOGIC FEATURES

Site of Lesion.—In many of the reported cases the exact, or even approximate, location of the lesion in relation to the distance above the dentate line or some other landmark was not mentioned; in many only the word "rectum" was used. However, in 68 cases sufficient description was given so that the height of the lesion could be fairly estimated (Table III). It can be seen that in 65 of the 68 cases the tumor was situated at, or in the vicinity of, the anorectal junction or else in the anus itself (Fig. 1).

TABLE III. LOCATION OF LESION IN SIXTY-EIGHT PATIENTS

LOCATION	NUMBER
Anus or anal canal	28
Anus and rectum or anorectal junction	12
Lower part of rectum, vicinity of anorectal junction	25
Rectum, 5, 6, or 7 cm. above anal orifice	3

These growths apparently do not tend to involve any one quadrant of the anus or rectum in preference to others. In 50 cases in which the involved wall

*Chalier and Bonnet knew of 8 additional cases, the details of which they could not procure; we know of 6 other cases, but are unable to obtain the journals in which they were described. Thus actually there are 108 known cases of this tumor.

was mentioned, the anterior wall was chiefly affected in 11 cases, the posterior wall in 19 cases, and the lateral walls (left or right) in 20 cases.

Gross Appearance.—The tumors are generally single, although 14 of the 94 lesions have been described as being multiple. They tend to be polypoid and to protrude into the lumen of the anus or rectum. In 19 of the 94 cases a definite pedicle was noted. The caliber of the intestinal tube is generally little affected. Ulceration has been noted occasionally, and the tumor in 1 of our cases was described as being "crateriform" (Case 7, Table I). In Hertzler's[17] case the

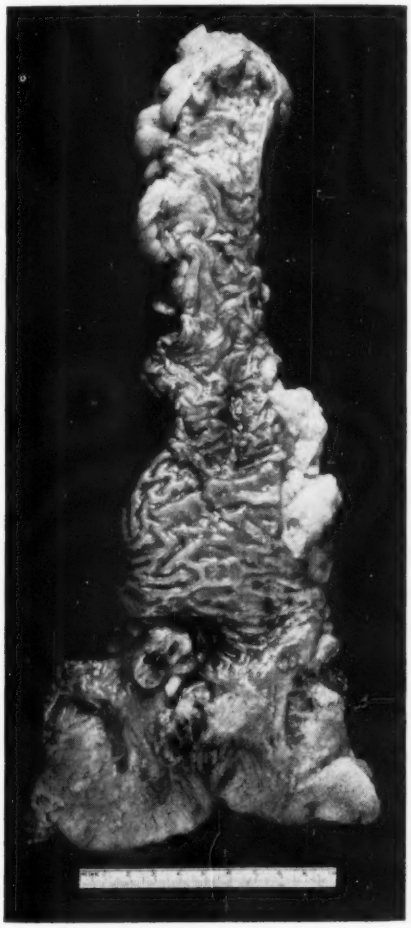

Fig. 1 (Case 10, Table I).—Note location of tumor in anus just above dentate line.

preoperative diagnosis was "thrombosed hemorrhoids"; similarly, in 1 of Smith and Broders' cases (Case 5, Table I) the gross appearance of the lesion suggested nothing more than "hemorrhoids and anal scarring." In another of our cases (Case 8, Table I), the lesion was simply a very small, benign-appearing polyp which was snipped off in the postoperative dressing section after the patient had had a ventral hernia repaired.

The size of these neoplasms varied from that of small miliary nodules to that of fist-sized masses. They were generally fairly small when diagnosed,

probably because their low position in the rectum resulted in early production of symptoms. Some of the descriptive terms which have been employed are lemon-sized, pigeon egg, small tomato, orange, half dollar, walnut, cherry, and bunch of grapes. In 5 of the 10 cases listed in Table I, the estimated diameter of the lesion was within 2 to 5 cm.

The color of the tumors described in Chalier and Bonnet's series of 64 cases varied from blue to frankly black to violaceous, some of them having only black plaques or specks on the surface; almost all of the lesions were described as being pigmented to a greater or lesser degree. In contrast, of the 30 cases reported since that time, in only 8 has definite pigmentation been noted on gross examination of the surface of the tumor; 2 of these tumors were black, 2 had "spotty pigmentation" or pigmented areas, 2 were blue, 1 was grayish, and 1 was dark brown. Presumably, many of the others have been colored like normal mucosa, since a good number of the preoperative diagnoses were anal or rectal "polyps."

The consistency of these growths was seldom mentioned in the case reports. Chalier and Bonnet stated that the tumors with pedicles were generally firm in consistency, but that this was "less uniform in the sessile growths."

Microscopic Appearance and Pathogenesis (Fig. 2).—Chalier and Bonnet noted that many authors had described the rectal tumors as arising, not in the mucosa, but in the submucosa of the rectum. McGuire and Leahy[23] and Kraker[20] described the malignant lesions as being in the submucosa in their cases, and in Goldman's[16] case the photomicrographs clearly show the melano-epitheliomatous tissue underneath the normal mucosa of the anorectal region, although the location is not described as such in the text. In Chalier and Bonnet's case the tumor seemed to arise directly from the malpighian epithelium of the anus, and these authors stated that all of the primary melanotic tumors of the anorectal region were in reality cutaneous epitheliomas coming from the anus, capable of becoming clinically tumors of the rectum by progressive orad infiltration along the submucosa, becoming pedunculated or secondarily ulcerated in the rectum.

Vickers[1] studied the tissue in 6 of the cases listed in Table I from the standpoint of their histopathology. He found that in 3 of the cases there was no demonstrable connection between the anal epidermis and the tumor. In Case 6 there was an apparent approximation of tumor and epithelium, although no direct connection could be definitely observed microscopically. In Case 5 there was a direct connection between tumor and epithelium, and photomicrographs showed the transition from the melanoblasts of the basal layer of the epidermis to those of the dermis, where they assumed an alveolar arrangement. In Case 3 the tumor extended from the anus into the rectum submucosally, with definite evidence of origin in the anal epidermis.

SYMPTOMS

Most of these patients considered their trouble to be of only a few months' duration. In the last 30 cases described, the average duration of symptoms before diagnosis was 9.2 months; in 2 cases symptoms had been present for four years or more and in 1 case for two years.

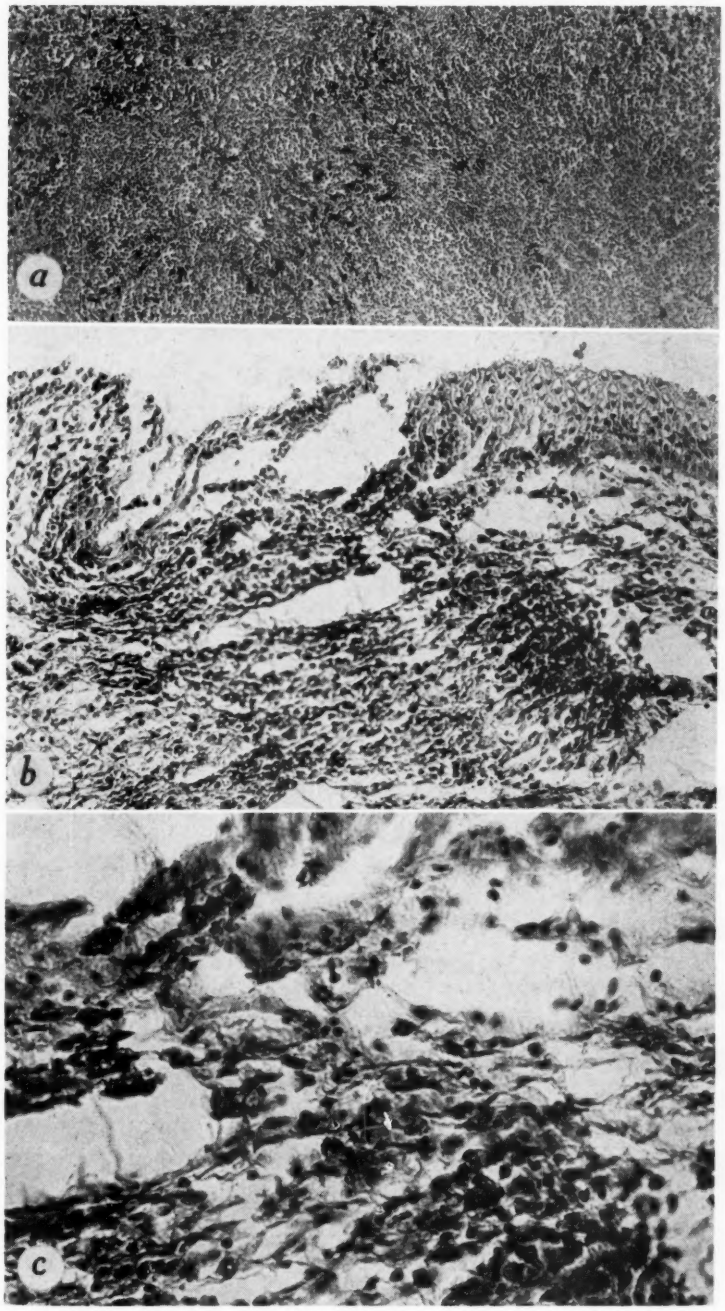

Fig. 2 (Case 10, Table 1).—*a*, Section of main portion of tumor showing characteristics typical of melano-epithelioma (hematoxylin and eosin ×60). *b*, Longitudinal section through mucocutaneous junction, showing close proximity of the malignant cells to the squamous epithelium of the anus (hematoxylin and eosin ×150). *c*, Same as in *b* (hematoxylin and eosin ×340).

The chief complaints were those associated with a tumor in the lower part of the rectum or anal canal; namely, anal pain, stool urgency and frequency, tenesmus, "full sensation" in the rectum, or rectal discharge. A tumor of, or a protrusion from, the anus was noted by 13 of the last 30 patients, and Chalier and Bonnet noted this tendency by describing a "tumor form" and a "prolapse form" among the modes of onset of symptoms. These authors also emphasized the frequency with which these lesions caused rectal bleeding, and this symptom has been described in 15 of the cases reported since their article.

In 2 of the 94 cases the presenting symptom was enlargement of an inguinal node, and in 5 cases there were either no symptoms or only general complaints such as poor appetite, loss of weight, and so forth. Constipation was complained of in only 5 of the 94 cases.

PHYSICAL FINDINGS

Only occasionally does the patient show cachexia, hepatomegaly, or other signs of metastasis upon diagnosis of the rectal lesion. In a few cases the tumor has spread to involve the inguinal nodes, which are palpable clinically at the time of the initial examination.

Local examination made digitally or proctoscopically is of course the best means of diagnosis, and this type of examination is seldom neglected because the patients have definite rectal symptoms. The usual diagnosis is rectal polyp, rectal polyp with malignant changes, or carcinoma until biopsy or microscopic study of the excised lesion establishes its true nature. Those growths which are deeply pigmented may be mistaken for thrombosed hemorrhoids or gangrenous rectal polyps.

TREATMENT AND RESULTS

Of the 94 patients, 72 (76.6 per cent) underwent surgical treatment. In 61 of these a definitive procedure, that is, removal of the tumor, was done; in the other 11 patients operated upon, either no attempt was made to remove the growth because of distant metastasis or local extension, or else the description of the operation failed to mention the type of procedure carried out. In 34 instances the operation consisted of more or less limited local removal of the growth, such as local excision, cutting of the tumor from its pedicle, cautery excision, or removal of the tumor and a small part of the anus with preservation of the sphincter. In 23 cases a radical excision of the rectum was performed, consisting generally of a combined abdominoperineal operation in either one or two stages. In 6 of the former and in 2 of the latter group, roentgen or radium therapy was used in addition. Finally, in 4 cases rectal extirpation was combined with excision of the inguinal lymph nodes. The long-term or the immediate postoperative survival rate did not vary, regardless of the type of surgical treatment used or whether or not radiation therapy was also employed. It should be noted in this connection that Goldman's[16] patient had only partial surgical removal of the growth because she refused more radical treatment, and treatment consisted of roentgen therapy and local implantation of radon seeds; she died in twenty-one months. Wilkie's[6] patient had two recurrent lesions treated with radium in addition to radium implantation at the time of the orig-

inal local excision; she was living and well two years and eight months after excision of the tumor.

Seven of the 72 patients operated upon died immediately after operation; of the 65 who survived, 53 have had follow-up studies done. Of the 53, 36 succumbed one month to six years postoperatively, with an average survival period of fifteen months. Seventeen were living, but 9 of these 17 had local recurrence or distant metastasis two months to three and one-half years postoperatively. Thus only 8 patients were known to be living and clinically free of the disease (Table IV). It is obvious that follow-up study was done on only 3 of them for such a length of time that they could be called "cured."

TABLE IV. DATA ON EIGHT PATIENTS REPORTED LIVING AND WELL

AUTHOR	YEAR	AGE (YEARS)	SEX	LESION		FOLLOW-UP PERIODS (MONTHS)
				SITE AND DESCRIPTION	TREATMENT	
Esmarck[3]	1875	31	F	Anus. Size of infant's fist; ulcerated	Excision of tumor and most of anus	132
Breuer[4]	1892	66	M	Posterior commissure of anus. Apple-sized; ulcerated; large pedicle	Tumor cut from pedicle	10
Smith and Broders[2]	1935	39	M	Anus. Found on routine examination of hemorrhoid tissue	Local excision	100
Lindner and Wood[5]	1936	53	F	Anorectal juncture, posterior wall. Indurated; two-thirds of circumference involved	Radical perineal excision of rectum	8
Wilkie[6]	?	?	F	Rectum. Papillomatous	Local excision and local radium therapy; 2 recurrences, treatment with radium	32
Chisholm[7]	1937	68	F	Anterior anal canal. Bluish, broad base, "Concord grapes"; bled easily	Radical posterior resection	30
Case 8 (Table I)	1937	52	F	Anus. "Small polyp"	Local excision	100
Case 10 (Table I)	1947	61	M	Left anterior dentate margin. Polypoid, firm, pigmented areas, submucosal infiltration	Radical posterior resection	4.5

SUMMARY AND CONCLUSIONS

Eighty-six cases of melano-epithelioma of the anus and rectum have been described in the literature up to the present writing. We have added 8 more cases, 1 of which was recently encountered by us. These lesions almost always occur in the vicinity of the dentate line, are frequently pedunculated, tend to be small, and are often covered by normal-appearing mucosa. They probably arise from melanoblasts of the anal epithelium, and location of the tumor in the rectum may be due to submucosal spread from the anus. Symptoms are generally produced early, and the diagnosis of "polyp" or "carcinoma" is frequently made on proctoscopic examination. Prognosis is uniformly bad, regardless of the type of therapy, there being only three known "cures" in the entire group of 94 patients.

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THE EVOLUTION OF NEUROSURGERY

ALFRED W. ADSON, M.D.,* ROCHESTER, MINN.

IN REVIEWING the evolution of neurosurgery I will attempt to present the subject in much the same manner that Judd employed in discussing a surgical subject. He was not given to lengthy discourses on historical backgrounds but employed the direct attack. His co-authors prepared the pathologic material while he evaluated the problem and emphasized the factors responsible for the progress in the treatment of a particular lesion.

Neurosurgery, which includes surgical procedures employed for the removal of neoplasms, to relieve pain, to treat inflammatory lesions, to suture severed nerves, to perform plastic operations, and to correct abnormal physiology of the autonomic system and brain, has developed as a special field of surgery within the last fifty years. Its greatest growth has taken place within the past twenty-five years.

However, surgery on the cranium dates back to the ancient Egyptians, Romans, and Peruvians who trepanned skulls to give egress to the evil spirits within. Traumatic cranial surgery undoubtedly was practiced during the various epochs before modern antiseptic and aseptic surgery were introduced, since the records show that this type of surgery was practiced during the Napoleonic wars. Attempts at removal of tumors from the skull and brain have been recorded since 1831 (Heyman). The first successful removal of a brain tumor by use of the Lister antiseptic technique is accredited to Richmond Godlee of London, who removed such a tumor on Nov. 25, 1884, the tumor having been diagnosed by Bennett and localized by neurologic methods. Macewen, as early as 1876, had diagnosed a brain abscess of the frontal lobe on the basis of contralateral hemiplegia. He advised surgical treatment which was refused by the child's parents. The autopsy verified his opinion. Macewen had operated on patients for brain tumors prior to Godlee's successful operation in such a case, but he had relied on certain cranial signs for localization rather than on neurologic findings. Ferrier, in discussing Godlee's paper, reported a case in which he had diagnosed a brain tumor by neurologic means. Weir of Philadelphia, on Nov. 17, 1887, is accredited with being the first American surgeon to operate on a patient for a brain tumor. Keen in 1891 reported five cases in which he had performed cranial operations. C. H. Mayo reported two cases of brain abscess in 1891.

Keen in 1895 commented on the fact that in spite of the rapid progress and brilliant achievement of modern antiseptic surgery, cerebral surgery had made but little advance until 1886 when Horsley and Macewen introduced radical changes in surgical technique. He stressed the importance of disinfection, urging that the head be shaved one day before the operation and that it be well scrubbed with soap and water before applying ether and the 1:2,000 solution of mercury bichloride. He emphasized the importance of the precept that the

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*Section on Neurosurgery, Mayo Clinic.

surgeon's arms, hands, and fingernails be thoroughly cleansed and that the instruments and dressings be scrupulously clean. He referred to the Wagener-Wolfe osteoplastic flap, but advocated removal of the bone overlying a tumor by cutting the bone between the trephine openings. He closed the skin flap without replacing the bone, waiting until the time of a secondary operation for such replacement. The dura was closed with sutures of catgut, and the skin with interrupted silkworm gut. The wound was covered with ample sterilized dressings which were kept in place by wet bandages covered with muslin bandages.

In 1896, Keen presented another paper entitled "The Surgical Treatment of Intracranial Tumors," in which he reviewed the status of brain surgery. He complained of ineffective methods of localization of cerebral tumors and emphasized the importance of having the co-operation of a neurologist and an ophthalmologist in consultation. He expressed a belief that the roentgen rays, which had come into moderate use, should offer aid. In reviewing the various types of craniotomy he stated that the Wagener-Wolfe method consisted of exploration by means of raising an osteoplastic flap over a circumscribed area. Horsley, in employing the osteoplastic flap, cut the bone between the four trephine openings with a straight saw. Krause changed this technique by employing a motor-driven circular saw, and Cryer employed a motor-driven circular osteotome in cutting the margins of the bone flap. Doyen advocated a more radical procedure in that his osteoplastic flap amounted to hemicraniotomy. Keen said that if the tumor were small, the operation should be completed in one stage, but if it were large it would be better to divide the operation into two stages. He advocated that Horsley's bone wax be used for the control of venous bleeding along the cut margins of the skull, that the meningeal vessels be ligated, and that only venous oozing be controlled by gauze packs. He again advocated removal of the bone flap if the tumor was inoperable and the employment of drains only when necessary, such drains to consist only of packs of iodoform gauze. He still adhered to the double closure of the wound, removing the table of bone at the first operation and replacing it one month later. If it were unwise to replace the table of bone, he suggested the wearing of a skullcap lined with a tin plate to protect the defect. In discussing the closure of bony defects he advocated the use of Koenig's method of transplanting a pedicled flap with the outer table of bone from an adjacent area to the defect, permitting the newly denuded area to granulate until Thiersch's skin grafts could be applied. He stated that Macewen used for replacement the bone fragments which were rongeured away at the time of the operation, while he substituted fragments of bone from the outer table in a normal area. Frankel, in 1887, suggested the closing of defects by the insertion of disinfected celluloid plates.

During these days of pioneer development, von Bergmann, in 1898, reported his surgical experiences with tumors of the brain. His cases and those of others reported up to that time made a series of 273 cases; 61.9 per cent of the patients had died and only 38.1 per cent had survived operation. He frankly confessed that the mortality rate was too high and that it would be lowered when improvements were made in localization of cerebral tumors and in surgical technique.

It is interesting to note that neurosurgery made greater progress when surgeons restricted their field of surgery to neurosurgery and devoted more time to neurology, neuropathology, and roentgenology, or when they were intimately associated with specialists in these fields.

The prophesies of Keen, Horsley, and von Bergmann have been fulfilled, since the surgical mortality rate following craniotomy has been greatly reduced and the results have become infinitely better as knowledge of localization has advanced and the surgical technique has improved. Harvey Cushing has been the chief exponent of these present changes, and he has urged that the neurosurgeon be a neurologist as well as a surgeon and that he be specially trained to carry out the delicate operations. In 1908, he presented a comprehensive review, "Surgery of the Head," in which he called attention to the changes made in the surgical technique. While Horsley still employed chloroform in conjunction with morphine as an anesthetic, he advocated etherization and the use of local anesthesia in selected cases. He referred to the use of the Heidenhain stitch for controlling bleeding of the scalp, but chose to use Esmarch's bandage. During this period the Toison chain saw in 1891 and the Obalinski-Gigli flexible wire saw replaced the chisels and gouges in elevating an osteoplastic flap. He accepted the Gigli saw as the best and employed Doyen's burrs in making the trephine openings. Cryer's spiral osteotome was still employed by some surgeons, DeMartel and Frazier being its chief exponents.

Dahlgren and De Vilbiss devised instruments for cutting the skull after a trephine opening had been made, and they employed this procedure for elevating an osteoplastic flap. Cushing recommended the Dahlgren forceps for narrowing the edges of the bone flap at the base. He employed Horsley's bone wax for controlling bleeding and described electrodes for stimulating the cortex to determine localization. He introduced the present method of closure of the scalp with interrupted silk sutures in the various layers. He has presented numerous monographs on the physiology of the brain and on the pathology of tumors, and has introduced many innovations in the surgical approach to, and removal of, tumors.

One of the most valuable innovations in the field of neurosurgery has been the introduction and use of the electrosurgical unit. This unit is a modification of Pozzi's fulguration apparatus, by Bovie, who combined a coagulation or diathermy unit with a desiccating, cutting unit in the same machine, so that it was possible to switch from one current to the other over the same electrode, thus making it possible to remove tumors piecemeal and instantly to have in readiness a coagulating current for control of bleeding. This appliance has made it possible to increase the scope of neurosurgery to include a large group of benign tumors situated in inaccessible places. The electrosurgical unit has also expedited resection of infiltrating tumors, and has facilitated control of hemorrhage during lobectomy. Frazier, Elsberg, Sachs, Mixter, Taylor, and many others in this country and abroad have likewise contributed to the refinement of the surgical technique.

During the pioneer days of brain surgery, the men of medicine were seriously concerned about the diagnosis and localization of cerebral lesions. However, they often were more concerned with methods of performing a craniotomy and controlling hemorrhage than they were with methods of tumor removal. Surgery was passing through the transitional stage from antisepsis to asepsis. The gentle handling of tissue and the perfect control of hemostasis were the result of Halsted's teaching. The increasing knowledge of anesthesia and of methods of administration of anesthetic agents aided in lowering the mortality. The postoperative care of patients was conducted with little or no knowledge of the physiologic processes responsible for cerebral edema or increased intracranial pressure.

As time progressed, many of us restricted our surgical efforts to the field of neurosurgery. By limiting our activities to the study and treatment of diseases affecting the brain, spinal cord, and nerves it became apparent that many lesions unrecognized or thought to be inoperable were amenable to surgical intervention. This increased the scope of surgical possibilities. It has encouraged several hundred men and women to devote their professional lives to this special field of surgery.

The progress made during the last twenty-five years has been due to many factors. The foremost of these has been the challenge that this problem has offered young men during their undergraduate and graduate years. It has been obvious that this special field presented research problems in diagnosis, surgical techniques, anatomy, pathology, physiology, electronics, and biochemistry.

DIAGNOSIS

The diagnosis and localization of cerebral neoplasms have progressed in accuracy as physicians and neurologists have learned the symptoms that are produced by expanding lesions within the brain. Experimental studies in physiology conducted by such men as Bernard, Horsley, Jackson, Foerster, Sherrington, Fulton, Penfield, Davis, and many others have contributed much to the localization of cerebral function which in turn has aided neurologists and neurosurgeons in the diagnosis and localization of cerebral neoplasms. Also, the ophthalmologist has become an important member of the diagnostic team. It is he, through his funduscopic examination and perimetric studies, who has been able to determine whether or not the papilledema is due to increased intracranial pressure or whether the optic atrophy is the result of the previous occurrence of choked disc or is due to pressure on an optic nerve by a pituitary tumor or a meningioma. The changes in the perimetric field, which may vary from a unilateral field defect to bilateral hemianopsia or homonymous hemianopsia, give further evidence of neoplastic localization.

Furthermore, the increasing knowledge of the roentgenologist has made it possible to demonstrate evidence of increased intracranial pressure on the basis of absorption of the clinoid processes and digitations in the skull. They have further revealed hyperostoses and bony destruction of the skull that accompany meningiomas. The roentgenograms likewise reveal deposits of calcium in certain

gliomas, meningiomas, and vascular lesions. Erosions of the porous acousticus and the shifting of the pineal body give further evidence of localization.

The pneumoventriculogram and the pneumo-encephalogram devised by Dandy have become of great value in the localization of brain tumors. These ventriculograms have proved to be of material value in differentiating non-neoplastic lesions from those that are neoplastic. They have also proved of value in localizing brain tumors in silent areas of the brain and in diagnosing lesions that have been too small to produce localizing signs other than those of increased intracranial pressure such as headache, projectile vomiting, and early papilledema.

Electro-encephalography is another physical and electronic diagnostic aid, since it reveals irregularities in the Berger rhythm in the presence of a brain tumor. At present it is not as reliable a test as pneumoventriculography but its value as a diagnostic aid will probably increase as our knowledge increases in the interpretation of the various graphs produced by the various lesions within the cranium.

The most recent chemical and physical aid in the diagnosis and the differential diagnosis of cerebral neoplasms is employment of fluorescein as devised by Moore at the Department of Surgery at the University of Minnesota. Moreover, Peyton has found the fluorescence of brain tissue to be a very valuable aid in the determination of the degree of spread of infiltrating tumors. It consists of an intravenous injection of fluorescein which collects in tumorous tissue and takes on a yellow hue when the neoplasms are exposed to an ultraviolet light. The chemical achievements of Moore who also has combined iodine isotopes with the fluorescein give further promise of localizing brain tumors with a Mueller-Geiger counter. It is hoped that electro-encephalography and use of the fluorescein isotope preparation can be further improved in respect to their diagnostic value since either procedure produces less discomfort than does pneumoventriculography. It is also hoped that they may be of value in diagnosing and localizing tumors in their early stage of development.

SURGICAL TECHNIQUES

The surgical techniques for craniotomy, subtotal and total removal of tumors, resection of lobes and decompression have become rather standardized during the last twenty-five years. Scalp hemostasis is now effected by the use of either pointed forceps on the galea or scalp clips. Osteoplastic flaps designed to preserve the circulation of the scalp and the supply of blood to the bone flap are rather universally employed in exposing cerebral cortex and neoplasms. Silver clips along with electrocoagulation are employed for the control of hemorrhage from smaller blood vessels. Gentle dissection and the frequent use of the electric loop with the high frequency current are essential steps in removal of a tumor. Bone flap and scalp closures are obtained by re-apposition and permanent fixation of the bone flap with tantalum wire and interrupted silk ligatures in the galea and skin.

Specially prepared instruments such as spatulas, guides, forceps, scissors, burrs, Gigli saws, and illuminated retractors and rongeurs have contributed

much to the facility of gently exposing brain tumors and the section of certain cranial nerves. The employment of modern tables and headrests has provided additional comfort for the patient and better exposure of surgical fields during the operation.

ANATOMY

Anatomic studies by such men as Rasmussen, Ranson, Fulton, and Kuntz and others are responsible for increasing the scope of neurosurgery. The better understanding of the cerebral circulation, anatomic centers, and corticospinal and sympathetic nerve tracts makes it possible to advise and perform operations for a variety of lesions. The newer operative procedures have consisted of angiography, tractotomy, lobotomy, and cortical resection. Angiography has aided the neurosurgeon in localizing aneurysms and other vascular lesions and in differentiating the same from neoplasms. Tractotomies, several in character, have been employed to section fibers and tracts for the relief of pain. Lobotomy, a procedure still in its infancy, was devised by Moniz and is employed to alter the mental states in certain types of insanity. It is also being employed to relieve pain wherein the pain complex is anticipated to be of psychogenic origin. Block resections of the cortex as employed by Foerster, Penfield, Cone, and Pilcher have been performed for the removal of scar tissue in epileptic patients. Premotor block resection of the cortex has been performed with the hope of relieving the spasticity and tremors of Parkinson's disease. It has also been used in the place of lobotomy to alter mental states in certain types of psychosis.

NEUROPATHOLOGY

Neuropathology in its early phase attempted to differentiate benign from malignant lesions of the brain, meninges, and peripheral nerves. The second phase consisted in developing an elaborate system of classification. Gliomas were divided into many groups even though all were infiltrating tumors. Meningiomas, likewise, were classified according to location, vascularity, the amount of fibrous tissue, deposits of calcium, construction of whorls, the presence of mitotic figures, and the presence or absence of invasion of bony tissue. The third phase of neuropathology consisted in a study of the life cycle of the tumor growth and the effects the tumor produced. Attempts were made to evaluate the duration of growth prior to the appearance of clinical symptoms, the rapidity and the character of the growth, the effects of subtotal and total removal, and the influence of irradiation on survival periods. Men like Cushing, Bailey, Penfield, and Kernohan have contributed much to our knowledge not only of classification of tumors of the brain but also of the life history of such tumors.

Still another phase of neuropathology is in the making and this has to do with the simplification of the classification of brain tumors. Instead of employing a great variety of classes, it is hoped, for example, that gliomas may be graded on a basis of malignancy, grading them on a scale of 1 to 4 in which grade 1 indicates a slow-growing tumor and grade 4 a tumor of rapid growth and of extreme malignancy. The study goes on further to evaluate the effects of surgical treatment and irradiation on the survival periods in order to deter-

mine whether the grade assigned at the time of operation can serve as a guide for the neurosurgeon in planning his operative procedure. This new phase of neuropathology is comparable to the method used in general pathology which guides the general surgeon in the treatment of neoplasms.

BIOCHEMISTRY

Marked advances were made in all branches of surgery with the introduction of aseptic surgery. However, nothing was so disastrous as when sepsis occurred after cranial operations, and for that reason extreme precautions were taken during operations to prevent sepsis. With the introduction of the sulfonamides and the antibiotics such as penicillin, streptomycin, and gramicidin a new era has appeared. Brain abscesses have almost become extinct as a result of the judicious use of the sulfonamides and penicillin in the treatment of middle ear disease, mastoiditis, and infections of the frontal sinuses. Meningitis, too, is not the fatal disease that it once was. It is rarely necessary to employ these drugs in primary craniotomies but in the event a cranial wound requires reopening, penicillin and occasionally a sulfonamide preparation dusted onto the margins of the wound eliminate the possibility of sepsis.

LESIONS OF THE SPINAL CORD

The factors responsible for the progress in surgical treatment of lesions of the spinal cord are not unlike those responsible for the progress in cranial surgery. The increase of neurologic knowledge concerning the symptoms produced by tumors, protruded intervertebral discs, and other lesions that produce pressure on the spinal cord has facilitated their early recognition and surgical treatment. Fortunately, 80 per cent of intraspinal tumors are benign and are removable.

Again, we find that the introduction of certain physical and chemical tests has proved of value in making a diagnosis and in differentiating the lesions that occur within the spinal canal. On spinal puncture, the presence of a fluid block (Queckenstedt test), the presence of xanthochromia (Froin test), and an increase of protein all confirm the presence of a spinal lesion. Myelography with the aid of air, oxygen, or iodized oil, such as lipiodol or pantopaque, has given additional aid in the localization and differentiation of lesions within the spinal canal.

NEURALGIAS

The relief of the major types of neuralgia again was due to pioneer work in physiology, neurology, and surgical techniques. As advances were made, section of the nerve fibers replaced avulsion of the gasserian ganglion and avulsion of the ninth nerve. At present these operations consist of an intracranial subtotal or total section of the sensory root of the fifth nerve and total section of the ninth nerve.

Intercostal neuralgia has been relieved by subarachnoid injection of alcohol and by rhizotomy. Chordotomy, unilateral or bilateral, which consists of sectioning the spinal thalamic tract in the upper part of the thoracic portion of

the spinal cord, is resorted to for excruciating pains due to injuries of the lower part of the spinal cord and for intractable pain due to malignant lesions involving the lower half of the body. Causalgia, usually due to lesion of the median nerve, is frequently amenable to cervicothoracic sympathectomy. Painful amputation neuromas may be relieved by resection. Unfortunately, the so-called phantom limb is still a perplexing problem; however, it may be relieved by a contralateral lobotomy.

OTHER NEUROSURGICAL FIELDS

During the early development of neurosurgery, clinicians were largely concerned with neoplasms of the brain and cord, abscesses of the brain, and the relief of trigeminal neuralgia but as advances were made, other lesions were found to be amenable to surgical intervention. One of these was *glossopharyngeal neuralgia*, a neuralgia of the ninth nerve in which the trigger zone is situated in the tonsillar fossa and in which excruciating pain extends to the submaxillary region and the inner ear. Dramatic relief of pain was accomplished by an intracranial section of the ninth nerve, an operation which I had the privilege of devising.

Ménière's disease, a condition characterized by violent paroxysmal attacks of vertigo, likewise came within the scope of neurosurgery. Medical regimens offered palliative relief but it required either subtotal or total section of the eighth nerve in order to obtain complete relief. Dandy and McKenzie were chiefly responsible for the development of this delicate surgical procedure. Of late, a newer operation has been employed for the control of the vertigo. It is referred to as the Day operation, a procedure which obliterates the semicircular canals on the affected side.

Advanced exophthalmos which progresses to a state of proptosis with ulceration of the cornea and loss of vision has also been controlled in many cases by the so-called Naffziger operation, a procedure designed to decompress the globus and the retrobulbar structures by removing the roof and the lateral wall of the orbit.

Scalenus anticus syndrome associated with the presence or absence of a cervical rib and characterized by constriction of the subclavian artery and pressure on the brachial plexus has been relieved by a section of the scalenus anticus muscle at the location of its insertion on the first thoracic rib. I devised this procedure and found that it was more effective in relieving the symptoms than was a previous operation which was employed in removing the cervical rib by the posterior approach.

Rupture of the *intervertebral disk*, with a protrusion of the nucleus pulposus, is a lesion that was not recognized clinically until 1922. Prior to that, Smorl had observed these pathologic lesions but no clinical significance had been attached to their presence. I called attention to their significance when, more or less by accident, I found that the nucleus pulposus had been completely prolapsed, producing marked pressure on the fourth lumbar root. The observation was made during a laminectomy which was designed to section the sensory

component of the fourth lumbar root for the relief of low backache with extension of pain along the sciatic nerve. The cartilaginous mass was removed and the root was not sectioned. The symptoms disappeared and the recovery was complete. Slow progress was made in this particular new field until myelography, which now assists us in demonstrating these lesions preoperatively, came to our aid.

SURGERY ON THE AUTONOMIC NERVOUS SYSTEM

Surgical procedures upon the autonomic nervous system received their first stimulus from an operation performed by Jonnesco who removed the stellate ganglion with the hope of relieving angina pectoris. Jaboulay and Leriche were exponents of periarterial sympathectomy for vasospastic lesions of the peripheral arteries. Though these men had many followers, the results were not all that were hoped for. This was due to the fact that the innervation of the peripheral arteries was neither centrifugal nor centripetal but instead segmental, corresponding to the somatic distribution of muscles and nerves.

Investigative work remained more or less static until Hunter and Royal of Australia gave it a new impetus. They both were more or less concerned with experimental and clinical phases of plastic tone in muscles. However, in carrying out their investigation, Royal suggested and performed ramisections on the sympathetic nervous system, with the hope of relieving the spasticity of extremities. The suggestion of ramisection stimulated me to advocate and perform sympathetic ganglionectomy and trunk resection in the place of ramisection, since multiple ramisections were not always complete inasmuch as the gray rami are constant in neither number nor distribution. Though the operation was performed originally to reproduce the results that Royal had observed, it was soon learned that a by-product of the operation of bilateral lumbar sympathetic ganglionectomy and trunk resection was of greater value than any relief of spasticity since there resulted an increase in the skin temperatures and the disappearance of the function of sweating. It was definitely proved that the increase in skin temperature was the result of increased blood flow and vasodilatation. The operation was promptly employed for the relief of *vasospasm* in the treatment of such conditions as *Raynaud's disease*, *thromboangiitis obliterans*, and *intermittent claudication in arteriosclerosis*. Several modifications of the original operation have been devised, with arguments supporting each procedure; some hold that a preganglionic section has certain advantages over postganglionic section which includes the ganglion and trunks. *Hyperhidrosis* of the fingers and hands has been relieved by sympathectomy since gray rami to the peripheral arteries include sudomotor fibers which are sectioned when attempts are made to relieve vasospasm.

The greatest challenge to neurosurgeons has come with attempts to relieve *malignant hypertension* by *sympathectomy*. I performed the original operation, attempting to produce falls in blood pressure similar to those observed occasionally when spinal anesthetics were given. The operation consisted of *ventral root rhizotomy* from the sixth thoracic to the second lumbar root, inclusive, in order to include white rami carrying vasoconstrictor impulses to the large vascular bed below the diaphragm. Since then, the original operation has been

replaced by a variety of procedures, all designed to carry out the original idea. One procedure consists of a *subdiaphragmatic extraperitoneal resection of the splanchnic nerves* together with a portion or the whole of the celiac ganglion along with the aorticorenal sympathetic ganglion and the upper lumbar sympathetic chain including the first and second sympathetic lumbar ganglia. This particular procedure I have devised and prefer to use. Peet prefers to section the splanchnic nerves above the diaphragm. Smithwick advocates and performs a combination of these two operations which is commonly referred to as a thoracolumbar procedure. Grimson advocates a still more extensive operation in order to include all of the sympathetic chain on each side. Poppen and others are employing thoracolumbar sympathectomy but use different incisions, thus avoiding a section of the diaphragm.

RÉSUMÉ

I have attempted to emphasize certain factors responsible for the growth of this new specialty from one of brain surgery to that of neurosurgery. I have also attempted to emphasize that lesions which formerly were unrecognized or thought to be inoperable have become amenable to surgical intervention. The limits of this field of neurosurgery have not been defined and the possibilities for its growth will depend on research in the fundamental and the clinical sciences of medicine.

THE USE OF HYALURONIDASE WITH LOCAL ANESTHETIC AGENTS IN NERVE BLOCK AND INFILTRATION ANESTHESIA

CHARLES K. KIRBY, M.D., JAMES E. ECKENHOFF, M.D., AND JOHN P. LOOBY, D.D.S., PHILADELPHIA, PA.

(From the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania, the Surgical Clinic and the Department of Anesthesia, Hospital of the University of Pennsylvania and the Evans Dental Institute of the University of Pennsylvania)

THE popularity of regional anesthesia has been limited because of the inability of surgeons and anesthetists to deposit anesthetic solutions accurately and consistently along nerve trunks. Even skilled anesthetists cannot obtain adequate blocks in all instances. A method of increasing the diffusion of local anesthetic agents might, therefore, be of value in producing a higher percentage of successful blocks. In certain instances, increased diffusion might also be helpful in infiltration anesthesia. The effect of hyaluronidase in spreading the anesthetic action of local anesthetic agents has therefore been studied.

Hyaluronidase, the mucolytic enzyme which acts on the mucopolysaccharide hyaluronic acid, is now generally conceded to be the "spreading factor" of Duran-Reynals[1] and McClean.[2] Current knowledge concerning hyaluronidase has recently been reviewed by Mann and Lutwak-Mann,[3] and Myer.[4] Other clinical uses for hyaluronidase now under investigation are the reduction of the viscosity of fluid in pathologic joints[5] and in mesothelioma of the pleura and peritoneum[4]; the induction of pregnancy in infertility due to a low hyaluronidase content of the husband's semen[6]; and the facilitation of absorption of fluid in hypodermoclysis.[7, 8] A survey of the literature has revealed that the idea of using hyaluronidase with local anesthetic agents has also occurred to Duran-Reynals[9] and Cosentino,[10] who did not record any experimental or clinical data.

EXPERIMENTAL OBSERVATIONS

Controlled experiments were done on volunteers (medical students) to determine whether a larger area of anesthesia results from the injection of hyaluronidase with local anesthetic agents and whether the duration of anesthesia is affected. The anesthetic solution without hyaluronidase was injected on the volar surface of the middle third of one forearm as a control. To 50 c.c. of the anesthetic solution to be injected into the same area of the other forearm, 0.8 or 1.6 mg. of hyaluronidase* were added. The hyaluronidase used in these experiments assayed to 150 provisional units per milligram by the turbidity reducing method of Kass and Seastone.[11] In the experiments in which vasoconstrictor was also used, 0.5 c.c. of epinephrine 1:1,000 was added to 50 c.c. of the anesthetic solution, with and without hyaluronidase. The needle was inserted just beneath the skin and 3 c.c. of the solution were injected without advancing the needle. At five and ten minutes after the injections the area which was anesthetic to pinprick was outlined and measured. Testing with pinpricks was continued until anesthesia disappeared and the time of disappearance was recorded.

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In Table I the increased area of anesthesia resulting from the spreading effect of hyaluronidase is shown. Deviation was not great in any subject, all measurements falling close to the average. In most instances in which hyaluronidase was used there was anesthesia extending distally to the hand, caused by blocking of cutaneous nerves. Measurements of the area of anesthesia were made proximally and laterally to avoid those areas in which anesthesia was due to nerve block. An interesting observation, which appears less striking in actual measurements than in the impressions of observers, was that the degree of spread was greatest when epinephrine was added to the procaine-hyaluronidase solution.

TABLE I. SPREADING EFFECT OF HYALURONIDASE ON PROCAINE INJECTED SUBCUTANEOUSLY

NUMBER OF SUBJECTS	SOLUTION INJECTED*	AVERAGE AREA OF SKIN ANESTHESIA (SQ. CM.)
28	Procaine 1%	8.8
25	Procaine 1% + hyaluronidase	15.7
13	Procaine 1% + hyaluronidase + epinephrine	17.5

*See text for amounts and concentration of solutions injected.

In Table II the effect of hyaluronidase on the duration of anesthesia is shown, both with procaine 1 per cent and with a longer-acting agent, pontocaine 0.15 per cent. Since the anesthesia time was shortened by the addition of hyaluronidase (presumably because of more rapid absorption) a vasoconstrictor, epinephrine, was added to delay absorption, with the result that the period of anesthesia was not significantly different with and without hyaluronidase.

TABLE II. EFFECT OF HYALURONIDASE AND EPINEPHRINE ON DURATION OF ANESTHESIA

NUMBER OF SUBJECTS	SOLUTION INJECTED*	AVERAGE DURATION OF ANESTHESIA TO PINPRICK (MINUTES)
28	Procaine	32
25	Procaine + hyaluronidase	23
13	Procaine + epinephrine	188
13	Procaine + hyaluronidase + epinephrine	180
12	Pontocaine	58
12	Pontocaine + hyaluronidase	30
10	Pontocaine + epinephrine	262
10	Pontocaine + hyaluronidase + epinephrine	228

*See text for amounts and concentration of solutions injected.

During these experiments the following additional observations were made:

1. The spreading effect of hyaluronidase in increasing the area of skin anesthesia was less impressive when injections were made intradermally rather than just beneath the skin. It is presumed that this was due to a less effective action of hyaluronidase in the dermal and epidermal structures than in the more loosely-bound subdermal and subcutaneous tissues.

2. The conspicuous area of skin elevation caused by the injection of 3 c.c. of procaine just beneath the skin was scarcely apparent and disappeared within one minute when hyaluronidase was used.

3. Following injections of solutions containing hyaluronidase, erythema appeared within five minutes and the area of anesthesia corresponded very closely to the area of erythema.

4. When both hyaluronidase and epinephrine were used together with a locally acting anesthetic there was blanching of the skin rather than erythema, and the area of blanching demarcated the area of anesthesia.

5. A few subjects noted slightly more tenderness for twenty-four to forty-eight hours in the area where hyaluronidase was injected than in the control arm. There were no other apparent untoward effects which could be attributed to hyaluronidase.

6. A further increase in the area of anesthesia could be produced by massage toward the periphery. This was also noted by Duran-Reynals in experiments with India ink.[9]

CLINICAL EXPERIENCE

The procaine-hyaluronidase-epinephrine solution has been used to produce regional anesthesia for general surgical and dental procedures. Epinephrine has been omitted in digital nerve block because of the possibility of producing ischemic gangrene and because the duration of anesthesia required is usually brief. For general surgical procedures 31 blocks have been attempted, as follows: finger 7, toe 5, intercostal 5, brachial plexus 4, lumbar sympathetic chain 3, femoral and lateral cutaneous nerves 3, and deep cervical, stellate ganglion, wrist, and ankle, 1 each. In most instances the onset of anesthesia was prompt, and the degree and duration of anesthesia adequate. There have been 2 notable failures, 1 a wrist and 1 a brachial plexus block. The cause of these failures was not clear. In addition to nerve block, hyaluronidase has been successfully used with local infiltration anesthesia in 3 patients with acute ankle sprains, 4 with subdeltoid bursitis, and 2 with acute myositis. In 3 high saphenous ligations a subcutaneous injection at one point rather than extensive intradermal and subcutaneous infiltration, has provided satisfactory anesthesia.

Hyaluronidase has been added to procaine in producing anesthesia for dental procedures in 65 patients. Twenty-seven were mandibular blocks and eight were tuberosity injections. It is the opinion of one of us who gave these injections (J.P.L.) that the blocks were easier to obtain and that the anesthesia was more widespread and absolute than usual. There were no failures. In the remainder of the patients infiltration anesthesia was given, with easily obtained and widespread anesthesia resulting. When desired, the area of spread could be increased further by massage. The over-all impression was that the addition of hyaluronidase to the procaine-epinephrine solution added facility and depth to dental anesthesia.

DISCUSSION

It is evident from the experiments described that the anesthetic effect of procaine and pontocaine was spread by the addition of hyaluronidase. In the early experiments with procaine the shortened duration of anesthesia appeared to be a serious handicap to clinical use. Pontocaine, a longer-acting agent, was tried but the addition of hyaluronidase reduced the anesthesia time nearly 50 per cent. This was thought to be due to accelerated absorption similar to that which occurs when hyaluronidase is used in hypodermoclysis. Although the mechanism of accelerated absorption has not been explained, an attempt was made to counteract it by adding a vasoconstrictor (epinephrine). A pro-

longation of anesthesia time similar to that obtained when hyaluronidase was not used in the anesthetic solution resulted, indicating blocking of the accelerated absorption effect by epinephrine. The action of epinephrine on the spreading effect of hyaluronidase was of interest. It seemed likely that if a vasoconstrictor decreased the absorption effect it might also decrease the spreading effect. This did not occur. The spreading effect, on the contrary, appeared to be increased by epinephrine. Presumably this was because the rapid absorption caused by hyaluronidase prevented the maximal spreading which occurred when absorption was delayed by a vasoconstrictor.

The number of patients in whom hyaluronidase has been used for nerve blocks is not yet large. Further studies should clarify the advantages and limitations of hyaluronidase in producing various types of regional anesthesia. In some areas, for example, the presence of fascial planes may interfere with diffusion. This may account for our failures in brachial plexus and a wrist block. At present digital nerve block appears the most impressive with prompt anesthesia following the injection of 2 to 3 c.c. of solution on each side of the digit. The use of hyaluronidase appears to be clearly advantageous in nerve block and infiltration anesthesia for dental patients.

CONCLUSIONS

1. The addition of hyaluronidase to local anesthetic agents injected subcutaneously increased the area of skin anesthesia but decreased the duration of anesthesia, apparently because of accelerated absorption.

2. When epinephrine was added to local anesthetic agents the duration of anesthesia was approximately the same with and without hyaluronidase. In most instances epinephrine increased the spreading effect of hyaluronidase, probably by delaying absorption.

3. Evidence is presented which suggests that hyaluronidase may prove helpful in producing regional and infiltration anesthesia in surgical and dental patients.

The authors wish to express their appreciation for the helpful suggestions made by Dr. Robert D. Dripps and Dr. Paul Gyorgy.

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BLOOD LOSS FROM DONOR SITES IN SKIN GRAFTING PROCEDURES

David W. Robinson, M.D., Kansas City, Kan.

(From the Department of Plastic Surgery, University of Kansas Medical Center)

BECAUSE of the danger of shock attendant upon major skin grafting procedures, a study was carried out to determine the quantity of blood lost from donor sites during operation. The blood loss in thirty-five operations forms the basis of this report.

Studies made by Gatch and Little,[3] Coller and associates,[2] Nadal,[5] Pilcher and Sheard,[7] J. C. White and associates,[10] and M. L. White and Buxton[11] have shown surprisingly large losses of blood in major surgical procedures. Certainly the transfer of large areas of skin to cover extensive burns is a major procedure for a patient whose general state is often depleted.

METHOD

The simple method of weighing the loss of blood (Wangensteen[9]) on dry sponges was utilized. Dry surgical sponges were weighed in 100 Gm. lots on a scale accurate to 1 Gm. Immediately after cutting the graft, dry sponges were placed upon the donor site catching all or nearly all of the blood. As soon as all the grafts were taken, at the time of dressing the donor sites, the blood-soaked sponges were weighed with all the unused sponges of the same 100 Gm. lot. The difference in weight was recorded as cubic centimeters of blood lost. Some blood was spilled but never more than a few cubic centimeters. (For practical purposes 1 Gm. of blood can be considered 1 c.c.) The time from the original application of the sponges until weighing was noted in some cases.

The dermatome was used for cutting the skin grafts in this study because it was more accurate for measuring the size of the donor site and because the skin could be split at a uniform thickness. The surface area of a donor site of a full drum cut is 32 square inches or 200 square centimeters. The depth of the graft cut was recorded as well as the size, number, and locations of the donor sites. The patient's age, sex, state of nutrition, and preoperative hemoglobin were tabulated (Table I). The preoperative medication and type of anesthetic administered were compared as possible factors affecting blood loss.

FINDINGS

The weighed blood loss per patient ranged from as little as 15 c.c. from the donor site of one-half a dermatome drum to 590 c.c. from nine full drums. Only six patients lost a weighed total of more than 250 c.c. The average loss from donor sites per patient per operation was 140 c.c. To standardize the weighed loss for each patient according to the surface area denuded, the blood loss per drum was calculated by dividing the total loss from donor sites per patient by the number of drums cut. This blood loss per drum made a convenient unit of measurement for comparison. The average loss for all patients was 46 c.c. per drum.

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A consideration of several factors previously thought to affect blood loss from donor sites gave the following results:

1. *Depth of Graft.*—The depth of the grafts according to the gauge on the dermatome varied from .008 inches to .024 inches. Comparing the loss at different depths in three groups: (1) superficial, .008 inches to .014 inches; (2) medium, .014 inches to .019 inches; and (3) moderately deep, .019 inches to .024 inches; the average loss per drum in Group 1 was 44 c.c. (22 cases), in Group 2 was 39 c.c. (8 cases), and in Group 3 was 67 c.c. (4 cases). The thinner grafts were cut more frequently since most of the grafts were used to cover granulating surfaces. Nine of the thirty-five patients had clean wounds needing coverage.

2. *Sex.*—The sex of the patient made little difference in blood loss, women losing 42 c.c. per drum and men 46.4 c.c. per drum. There were 9 women and 26 men in this study.

TABLE I

NO.	AGE (YR.)	SEX	PRE-OP. HB. %	STATE OF NUTRITION	DONOR SITE	DEPTH OF GRAFT IN INCHES	NO. OF DRUMS	TOTAL BLOOD LOSS (GM. OR C.C.)	BLOOD LOSS PER DRUM (GM. OR C.C.)
1.	4	F	91	Good	Buttock	.014	⅔	50	75
2.	2	M	68	Good	Abdomen	.020	½	33	66
3.	48	M	76	Poor	Back & thigh	.012	7	193	26
4.	10	F	71	Good	Chest	.018	1	31	31
5.	9	F	84	Good	Abdomen	.020	1	12	12
6.	14	M	76	Good	Abdomen	.020	2	89	45
7.	19	F	93	Poor	Abdomen	.010	1	38	38
8.	19	F	74	Poor	Back & chest	.010	7	270	39
9.	17	M	86	Fair	Chest & abdomen	.010	3	170	63
10.	9	M	66	Good	Thigh	.018	1	22	22
11.	49	M	70	Good	Back & thighs	.010	9	590	63
12.	49	M	58	Fair	Back & thigh	.012	4	170	43
13.	5	M	70	Good	Back	.010	3	175	58
14.	55	F	72	Fair	Thigh & abdomen	.010	2	32	16
15.	15	F	78	Fair	Abdomen & chest	.012	3	170	57
16.	15	M	85	Fair	Back & leg	.012	7⅔	375	76
17.	48	M	74	Fair	Abdomen & thighs	.012	4	71	18
18.	20	M	84	Fair	Back	.012	1½	229	150
19.	4	M	68	Fair	Back & leg	.010	3½	223	64
20.	54	M	80	Good	Abdomen & thigh	.016	2½	49	20
21.	54	M	64	Good	Thigh	.016	½	15	30
22.	48	M	83	Fair	Abdomen & thigh	.010	5	69	14
23.	4	M	71	Good	Back	.012	1½	78	52
24.	20	M	91	Good	Thigh	.014	1½	92	61
25.	3	M	76	Good	Back	.008	1⅓	54	32
26.	17	M	85	Good	Back	.008	3½	274	78
27.	20	M	87	Good	Thighs	.020	3	102	34
28.	20	M	84	Good	Back & thigh	.024	2½	275	110
29.	40	F	70	Poor	Back & abdomen	.010	6	65	11
30.	82	M	74	Poor	Back & thigh	.008	4	40	10
31.	2½	M	73	Good	Back & buttock	.010	3	90	30
32.	40	F	70	Fair	Back & buttocks	.012	5	294	59
33.	40	M	71	Fair	Thighs, chest, & abdomen	.012	11	145	14
34.	69	M	71	Fair	Thighs & back	.012	4½	38	9
35.	11	M	74	Fair	Thighs & abdomen	.012	4½	78	17

3. *Donor Site Location.*—A comparison of the blood loss from different donor areas of the body was made because of the difference of thickness of the skin in various locations. Three different areas were compared: (1) the abdomen and chest, (2) the back, buttocks, and loins, and (3) the thighs. When two of these different locations were used, the results were not included in the analysis. Blood loss from the back and buttocks averaged 51 c.c. per drum, from the abdomen and chest 41 c.c. per drum, and from the thighs 38 c.c. per drum.

4. *State of Nutrition.*—Blood losses in patients of varying nutritional states were compared. The condition of these patients was classified as good, fair, and poor, according to their clinical appearance and their hemoglobin and plasma protein determinations. It was assumed that patients in a good state of nutrition would have more turgidity of the skin and thus bleed more readily than the poorly nourished patients with loss of elasticity of the skin. This was found to be true. The weighed loss per drum was 48 c.c. in the group considered good (17 cases), 45 c.c. in the group considered fair (13 cases), and 25 c.c. in the group considered poor (5 cases). The average blood loss per drum in patients whose hemoglobin was 80 per cent or more was 61 c.c., while for those patients below 80 per cent hemoglobin the average loss was 34 c.c.

5. *Age.*—Similarly, regarding tissue turgidity, the age of the patient as a factor in blood loss was considered. Whereas the average loss for all patients was 46 c.c. per drum, for children 10 years of age and under (10 cases), the loss was 44 c.c. per drum and for adults over 45 years of age (10 cases), the loss was 25 c.c. per drum.

6. *Anesthesia and Preoperative Medication.*—No significant comparison of blood loss with the various anesthetic agents employed could be made. Ether with or without nitrous oxide induction was employed in all but six instances, cyclopropane was used five times, and intravenous sodium pentothal once. Although cyclopropane has been said to cause increased bleeding at operation, the blood loss per drum when it was used was 36 c.c. compared to 49 c.c. for ether. As nearly all the patients in this study received the same preoperative medication, namely, morphine and atropine or derivatives, no comparison of blood losses could be made. One patient, an adult with a definite atropine flush, lost 229 c.c. from one and one-half dermatome drum sites on the back, the largest loss per drum (150 c.c.) in the series.

7. *Time Before Dressing Donor Site.*—The time factor was so variable that no reliable comparison could be made. Some donor sites were dressed five minutes after the graft was cut, but others were not dressed for fifty minutes. No donor sites were dressed until all the grafts had been taken. It was observed, however, that little to no bleeding occurred on removal of the blood-soaked dressings for weighing, regardless of the time which had elapsed, unless the sponges were removed under five minutes from the time of cutting or unless a large adherent clot was removed with the sponges before applying the first definitive layer of a grease gauze.

COMMENT

In general, the weighed blood loss from donor sites was less than expected. Some spilled blood and some further exudation of blood-tinged plasma under

the definitive donor site dressing if recorded would have increased the blood loss per patient somewhat, but probably not more than 20 per cent. The uncaught blood could have been accounted for had the colorimetric methods of determining blood loss been used but even then, according to M. L. White and Buxton[11] and J. C. White and associates,[10] there might have been an error of from 5 to 15 per cent.

Although it would seem logical for more bleeding to occur the longer the time interval between the cutting of the grafts and the application of the donor site dressings, such did not seem to be true from these observations. It was concluded that the blood clotted under the sponges at the coagulation time for the individual patient, allowing little further bleeding. Some of the fluid part of the blood absorbed on the sponges was lost by evaporation before weighing, especially in hot dry weather. A long time interval between the cutting and application of dressings would therefore give slightly lower blood loss figures.

Tissue turgidity proved to be a factor in blood loss. The well-nourished patient with skin somewhat tight over the subcutaneous fat bled more from the donor site than the emaciated patient with loose skin. For the same reason patients in the older age group bled less than younger patients.

Although there is some compensation due to greater contractibility of the vascular tree, the blood loss from donor sites in children is of relatively greater importance because of their lower percentage of blood volume to body weight than adults. In small children whose blood volume is 5 per cent of the body weight,[4] the loss of small amounts of blood is important. Adults with a blood volume of 7 per cent of body weight[6] can tolerate relatively greater blood losses.

Varying the depth of the graft produced different blood losses from donor sites as was expected. Skin split at one-half to two-thirds of its thickness bled more than superficial splits of from .008 inches to .012 inches. The actual depth of the graft cut may not be the depth indicated by the dermatome gauge because the thickness of the skin cement or drum cement layer and the amount of tension put upon the skin in raising it to cut the graft are unmeasurable factors. The degree of error in depth, however, is not great enough to alter comparison of the three groups of different depths here under consideration.

Different donor areas of the body bled different quantities. The skin of the back and buttocks, having a thick firm dermis, bled more than the skin of the abdomen, anterior chest, and thighs, probably because the back skin was less free and because its thick dermis did not contract around the open ends of the cut small vessels.

In no patient was the total amount of blood lost from donor sites considered to be sufficient in quantity to produce shock from hemorrhage alone. It must be remembered, however, that those patients debilitated from long-standing open granulations should not undergo prolonged operative trauma without good support to the blood volume. Further, the loss of blood from the recipient areas at the time of grafting, although not measured in this study, may be equal to, or greater, than the loss from donor sites. Many of these patients have a lowered total blood volume and suffer from "chronic shock," a concept clinically

considered for some time, and recently emphasized by Clark and associates[1] and by Ponder.[8] The transfer of large sheets of skin, totaling in surface area as much as 360 square inches in one operation as we find advisable to use in some cases, is a major undertaking and should be regarded as such, utilizing all safeguards for the patient's life.

SUMMARY

1. Blood losses from donor sites were determined in thirty-five skin grafting operations using the weighed-sponge method.

2. Total blood losses were not large, averaging 46 c.c. per dermatome drum of skin removed, the largest total loss being 590 c.c. for nine drums.

3. It was found that more blood was lost from (a) thick grafts than thin ones, (b) from the back and buttocks than from the abdomen, chest, and thighs, (c) from patients in a good state of nutrition than from the poorly nourished, (d) from younger patients than from those above 45 years of age.

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RUPTURE OF THE LEFT PECTORALIS MAJOR MUSCLE

Report of a Case

Major Edwin J. Pulaski and Major George W. Martin, Medical Corps
Army of the United States

(From the Surgical Research Unit, Brooke General Hospital Brooke Army Medical Center, Fort Sam Houston, Texas

ONE of us (E. J. P.), in 1941, reported a case of rupture of the left pectoralis major muscle.[1] A thorough search of the literature revealed only seventeen other cases reported. In the past six years three additional cases have been added to the literature,[2, 3, 4] bringing the total number reported to twenty-one. It is the purpose of this communication to present the findings and outcome in one additional case.

REPORT OF CASE

A white man, 31 years of age, employed as a telephone construction lineman, was admitted to the hopsital on Aug. 8, 1947, with a complaint of increasing pain and swelling of two days' duration over the left pectoral region. His work consisted of stringing telephone wires onto the crossarms of telephone poles. This work necessitated stretching one arm overhead (the left, usually) and adducting the arm while balancing on the pole with the other arm. On August 6, while at lunch, he noted sudden severe pain in the left pectoral region, which felt swollen. He recalled no undue incident while working. The swelling increased rapidly in size, and when he examined the area he noted a tumor measuring approximately six inches in diameter. He was unable to lift the arm above the level of the shoulder because of severe pain. The swelling increased progressively and the skin over the area assumed a bluish discoloration. By that evening the area of discoloration had spread until it extended over the left chest, the left abdomen, and into the left scrotum. Examination at the time of admission revealed marked ecchymosis and tumefaction over the left pectoral region, being most intense near the axillary fold, and radiating into the axilla and downward to the crest of the ileum, the penis, and the scrotum. The tumor was soft, warm, and very tender. No definite tear in the muscle could be determined. The patient was unable to abduct the arm more than 45 degrees, and complained of pain in the muscle on attempted adduction of the arm against resistance. A clinical diagnosis or rupture of the left pectoralis major muscle was made. Laboratory studies, including repeated complete blood counts, clotting time, and serology, were normal. Darkened blood, 10 ml., was aspirated from the hematoma, a culture of which yielded no growth.

While the patient was undergoing further studies, the arm was immobilized. Slow progressive disappearance by absorption of the extensive ecchymosis took place. The tumefaction in the axillary fold became somewhat smaller and less tender, but it persisted. Ten days after admission the patient still was unable to abduct the arm more than 60 degrees. A moderate amount of pain in the pectoral region on attempting to adduct the arm against force was present.

The patient was operated upon on August 21 under a pentothal anesthesia. An incision was made over the tumor along the anterior axillary fold through the skin and carried down through the fascia covering the pectoralis major. Semiclotted blood, 140 ml., was evacuated from the defect between the two muscle fragments. The wound was then thoroughly irrigated with normal saline solution, and the severed portions of the pars abdominalis were demonstrated at the superior and inferior portions of the wound. The tufted ends of the severed muscle measured about 2 cm. in diameter and were friable. Approximation of the severed ends of the muscle was deemed impractical because of the extent of the retraction (approximately 10 cm.), and the friability of the severed tissue.

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The overlying sheath was reapproximated with interrupted 00 chromic catgut sutures, and the skin was sutured with fine black silk. A tight, fluffy, pressure dressing was then applied to the area. The postoperative course was uneventful. The sutures were removed on the seventh postoperative day, and per primam wound healing was obtained. Subsequent to this the patient noticed progressive improvement in abduction with concomitant loss of pain on motion. Passive exercises and massage to the operative area were then instituted. By the time of discharge from the hospital, on Sept. 2, 1947, the patient was able to abduct the arm fully without pain. A slight residual weakness was present in the overall movements of the extremity. He has been able to resume his former work.

COMMENT

The important features of a case of rupture of the pectoralis major muscle are presented. The fact that two patients with such ruptures have been seen by one of us in a period of less than two years would indicate that this lesion is not so rare as suggested by the paucity of the reports in the literature.

The clinical diagnosis of rupture of the pectoralis major muscle is not difficult. The usual history is that of strong forcible adduction in the abducted position of the outstretched arm. Of the twenty-one cases in the literature, strong pull on the contracted muscle accounted for eleven tears, and five additional ruptures were due to a combination of strong pull on the muscle and direct blows by blunt, heavy objects. The causative factors in two cases were not stated. Of the three remaining cases direct violence was credited as the cause in one, and senility in two. Tumefaction and ecchymosis over the pectoral region are present in all cases. As the hematoma absorbs, indentation over the rupture site may be demonstrated. Attempted motion of the arm is usually accompanied by pain over the torn muscle. By having the patient attempt strong adduction against resistance the separation and swelling increase, the tumefaction hardens, and pressure over it causes pain. The degree to which adduction is possible is proportionate to the extent of the tear.

Surgical repair with evacuation of the hematoma is the treatment of choice for rupture of the pectoralis major muscle. The tear always involves the muscular portion of the muscle, usually near its tendinous insertion in the axillary fold. The pars abdominalis is most frequently affected, the pars sternocostalis less commonly. Tear of the clavicular portion is rare. Complete tears have not been reported. Conservative treatment may lead to spontaneous restoration of function, but this is slow and full power is never restored. Kingsley[4] saw a patient eight years after injury which had been treated conservatively. The pectoral fold was flattened, and a scar presented in the sternocostal area of the muscle. There was weakness of moderate degree, which was not incapacitating. This was explained by Kingsley as due to the minor role of the pectoralis major in ordinary use of the arm.

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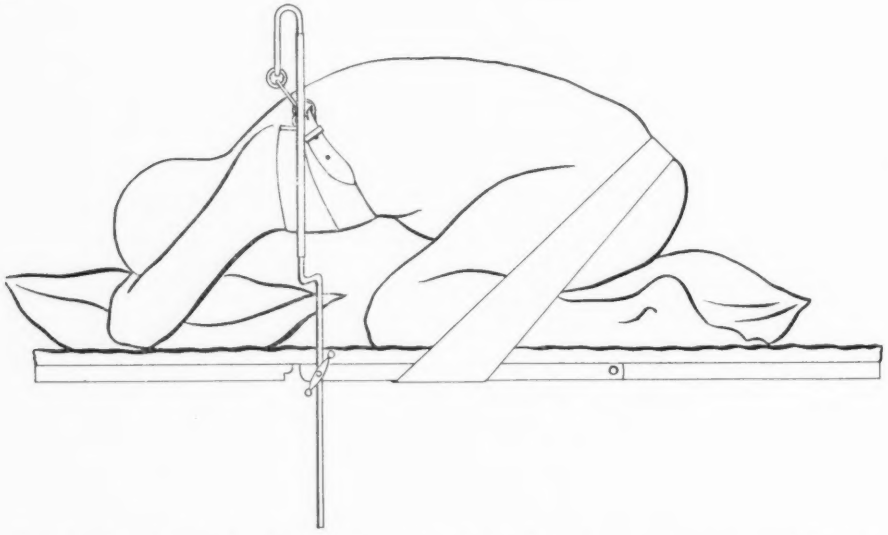
KNEELING POSITION FOR OPERATIONS ON THE LUMBAR SPINE

Especially for Protruded Intervertebral Disc

Arthur Ecker, M.D., Syracuse, N. Y.

FOR over two years I have used the kneeling position (Fig. 1) for all explorations of the spinal canal in the lumbar region. These eighty-three operations were mostly for protruded intervertebral disc. The kneeling position offers four advantages: (1) maximal space between the laminae; (2) *greatly diminished bleeding* from the epidural veins due to lack of pressure on the abdomen; (3) relaxation of the affected nerve root by maximal flexion of the knees; (4) maximal flexion of the bodies of the lumbar vertebrae, which is the ideal position for fusion of the bodies of the vertebrae themselves. Formerly, when the lumbar spine had been flexed by pressure under the abdomen, red and white blood cells were usually found in the urine for the first two or three days after operation. These cells have not been found since the kneeling position has been used.



To obtain the desired position, it is best for the patient to crawl onto the operating table. Anesthesia is administered only after the patient's chest is supported comfortably. Although both ether anesthesia and spinal analgesia have been used successfully, the anesthetists prefer intravenous pentothal supplemented with nitrous oxide-oxygen by inhalation. For muscular relaxation, small doses of curare are given intravenously. Tilting up the table slightly at the head end releases intestinal pressure against the diaphragm and makes breathing easy. Ordinary retractors and an overhead light are adequate for operating in this position.

I do not know who suggested this posture first, but was informed of it by Dr. John B. Stevens, an orthopedic colleague. He saw it used by Mr. Kenneth H. Pridie of Bristol, England, who in turn had learned it from Mr. McKee of Norwich.

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EXPERIMENTAL URINARY TRACT OBSTRUCTION PRODUCED BY CELLOPHANE SCLEROSIS

Report of a Method

George W. Duncan, M.D., and Willard E. Goodwin, M.D.,* Baltimore, Md.

(From the Department of Surgery and The James Buchanan Brady Urological Institute, The Johns Hopkins University and Hospital)

EXPERIMENTAL obstruction of the urinary tract, particularly hydronephrosis, has been a subject of long-standing interest among investigators. The work of Scott and Sullivan,[1] Keith and associates,[2, 3] and Hinman and his co-workers[4, 5] has contributed much valuable information concerning the anatomic and functional changes in hydronephrosis. In their experiments obstruction was produced by complete occlusion of the ureters with silk ligatures or by partial occlusion with rubber bands. The results of these workers showed their methods to be adequate, but the use of rubber bands was difficult to standardize, and the obstruction was not always slowly progressive.

The experiments of Page[6, 7] and of Graef and Page[8] showed that wrapping the kidneys with cellophane produced an intense, progressive, fibrotic reaction with subsequent renal ischemia and hypertension. Pearse[9] utilized this tissue reactivity to cellophane to produce gradual occlusion of the dog's aorta. This property of cellophane suggested to us the use of this material as an agent for producing slowly increasing urinary tract obstruction similar to that seen in man.

METHOD

Adult mongrel dogs (nine males and six females) weighing from 5.8 to 22.0 kilograms were used in fifteen experiments. Under sodium pentobarbital anesthesia (32 mg. per kilogram), the abdomen was opened through a lower midline incision, and the bladder neck or lower ureters were exposed. The cellophane was folded into a band four layers thick, 1 cm. wide, and of sufficient length to encircle loosely the ureter at the ureterovesical junction or the urethra at the bladder neck. In the first twelve experiments the cellophane band was tied in a knot which was held in place by a silk suture. In the last three experiments the bands were applied without tying, and loosening was prevented by mattress sutures in the bands. In all cases the cellophane was placed loosely enough about the ureters or urethra to admit the passage of a Kelly clamp under the band.

In the first twelve experiments unspecified commercial cellophane was used with good results. In the last three experiments the observations of Poppe and deOliviera[10] on the difference in reactivity of tissues to different types of cellophane were utilized. In these animals the ureters were first banded with highly

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*National Research Council Fellow in the Medical Sciences.

Fig. 1.

Fig. 2.

Fig. 1.—Bilateral hydroureter and hydronephrosis, in situ, produced in a puppy by banding of lower ureters with 300 P. T. DuPont cellophane.

Fig. 2.—Post-mortem urogram of the same specimen.

Fig. 3.

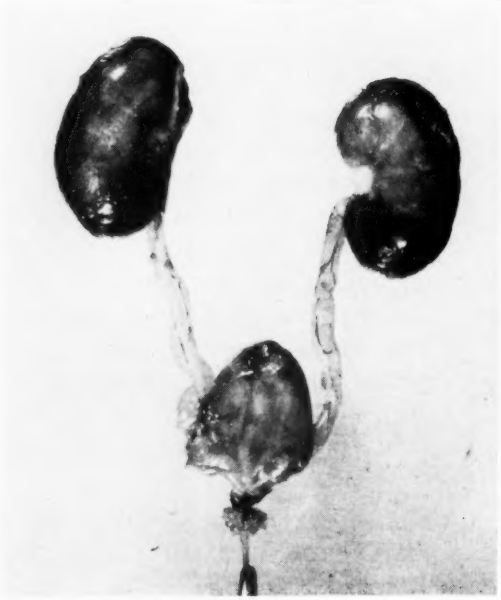

Fig. 4.

Fig. 3.—Vesical neck obstruction with minimal upper urinary tract damage but marked dilatation and hypertrophy of bladder, produced by banding urethra with cellophane.

Fig. 4.—Vesical neck obstruction, produced as in Fig. 3, producing bladder dilatation and hypertrophy and bilateral hydroureter and early hydronephrosis.

reactive polythene,* which was then loosely wrapped with the presumably non-reactive 300 P.U.T. 71 DuPont cellophane.* The cellophane was sterilized in alcohol for twelve hours. In one case it was autoclaved with subsequent marked shrinking of the polythene and the 300 P.U.T. 71 DuPont cellophane, making these materials very difficult to use.

In seven animals the cellophane band was placed at the vesical neck. In one animal a band was placed both at the bladder neck and about the lower left ureter. In two animals a band was placed about the left ureter alone, and in five animals both ureters were banded. The animals which had not died at the end of eight months were sacrificed or explored.

Hodges and Goodwin have since banded both ureters with commercial 300 P.T. DuPont cellophane in seven puppies for another type of experiment. In all of their animals severe, rapidly progressive ureteral obstruction and death from hydronephrosis occurred. The post-mortem anatomic findings in the urinary tract and a post-mortem retrograde urogram in one of these animals are shown in Figs. 1 and 2.

RESULTS

In seven animals in which a band was placed about the urethra, obstruction was observed in all cases. Four of these animals died after a period of 3½ to 6 months. The other three were sacrificed at the end of 8 months. All showed moderate to marked dilatation and hypertrophy of the bladder (Fig. 3). In two of these animals there was dilatation of both ureters and renal pelves (Fig. 4), and in one case there was unilateral dilatation of the ureter and renal pelvis.

In the animal in which a band was placed both at the vesical neck and on the lower left ureter there was moderate dilatation and hypertrophy of the bladder and an extreme degree of hydroureter and hydronephrosis on the banded side. The unbanded side remained normal.

Of the two animals in which a band was placed around the lower left ureter, one showed a moderate hydronephrosis while the other showed little change.

In the five animals in which a band was placed about both ureters, moderate to marked bilateral hydronephrosis and hydroureter were observed in all cases.

Observation of the tissue reactivity in the banded areas at autopsy or laparotomy demonstrated the same changes described in detail by Graef and Page[8] in their study of the pathology of cellophane perinephritis. There was variation in the degree of fibrosis, which can be correlated with the duration of the process. In one of the animals in which the combination of polythene for maximum reactivity and the covering of this with 300 P.U.T. 71 DuPont cellophane for protection of the surrounding tissues was used, there was definite obstruction and fibrosis but little reaction outside the immediate area. In this instance the cellophane films had been sterilized by autoclaving. In two similar experiments where the same technique was used and the polythene and cellophane were sterilized in alcohol for twelve hours, there was much greater reaction and therefore more obstruction.

*Supplied through the courtesy of the E. I. DuPont de Nemours Company, Cellophane Division, Wilmington, Del.

SUMMARY

A method is described for the experimental production of slowly progressive urinary tract obstruction by banding the ureters or urethra with cellophane. This produces a marked sclerotic reaction in the surrounding tissues and subsequent urinary tract obstruction due to gradually increasing fibrosis.

The use of different types of cellophane for this purpose is briefly discussed. It is concluded that either commercial 300 P.T. DuPont cellophane or the more reactive polythene is suitable for the experimental production of obstructive uropathy.

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A MATTRESS FOR PATIENTS WITH BOWEL FISTULA

W. S. Dempsey, M.D., and Thomas E. Jones, M.D., Cleveland, Ohio

(From the Cleveland Clinic)

MANAGEMENT of the patient with an ileostomy or a high small intestinal fistula is often complicated by excoriation of the skin around the fistula. In the Cleveland Clinic, aluminum paste and aluminum hydroxide gel* have proved valuable in treating this condition. However, in a few intractable cases it has seemed advisable to free the skin completely from contact with the irritating intestinal fluids. Bradford frames and sump drains have been tried with fairly good results, but recently a simple comfortable method has been employed with even more success.

In an ordinary innerspring mattress an opening 6 inches in diameter is made and lined with rubber sheeting (Fig. 1). This mattress is placed on a hospital bed which breaks in the middle, and the bed is made up with half sheets, exposing the opening in the mattress. A small (6 inch) enamel basin is placed in the hole. The patient lies face down on the bed with the fistula directly over the basin. If the fistula is flush with the skin, side-to-side motion is voluntarily restricted to prevent the drainage from contact with the skin. If the fistula is ½ to 2 inches in length (as is the usual ileostomy) the patient may roll to either side with reasonable ease, avoiding contact of the drainage with the skin. The patient of average build is comfortable in this position. The extremely thin patient may be made more comfortable by breaking the bed slightly in the middle.

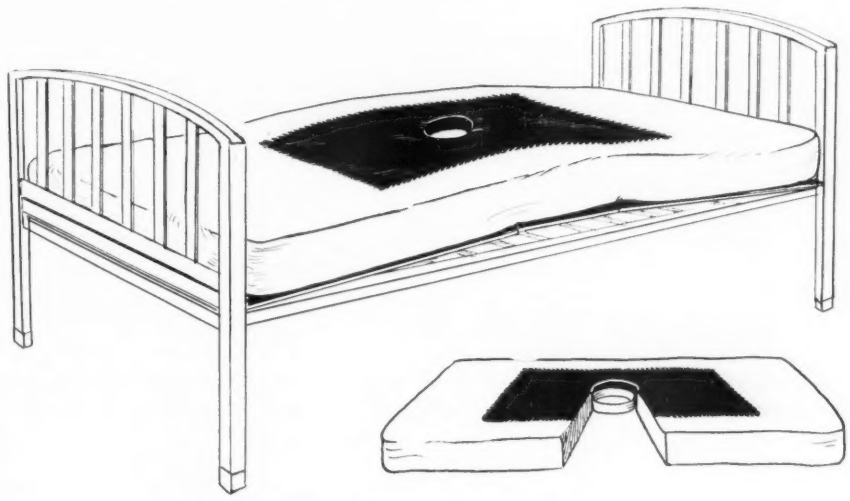

Fig. 1.—Mattress for patients with bowel fistula.

This device has proved most satisfactory, and gratifying improvement has taken place within twenty-four to forty-eight hours after the mattress has been in use. Patients with an ileostomy may use similar mattresses at home when necessary.

The authors wish to express their thanks to Mrs. Louise McLain of the Housekeeping Department for her cooperation in constructing these mattresses and to Miss Beatrice Boyle of the Art Department for her drawing of the mattress.

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GLOMUS TUMOR WITHIN BONE

WILLIAM LEHMAN, M.D.,* AND CORNELIUS KRAISSL, M.D., NEW YORK, N. Y.

(From the Surgical Pathology Laboratory, College of Physicians and Surgeons, Columbia University)

SINCE Masson's[1] original description of the glomus (neuromyoarterial) tumor, a good number of these neoplasms have been reported in the literature. Most of them were in the fingers, but occasionally they are found on the lower leg, arm, and elsewhere.

Lattes,[2] finding such a tumor within the terminal phalanx of the right thumb, carefully reviewed the literature from the time of the Masson paper but was able to locate only one other intraosseous glomus tumor, that of Iglesias de la Torre and associates[3] who reported such a neoplasm in 1939. Because so few glomus tumors have been reported in bone, it seems worth while to report two additional cases, both within terminal phalanges of the fingers. Both cases presented typical symptoms, completely relieved in each instance by simple curettage. In each case, the diagnosis was suspected from the symptoms and history, but the roentgenologists, unaware of the clinical findings, did not consider or mention the possibility of glomus tumor in either case.

CASE REPORTS

CASE 1.—C. A., a 48-year-old housewife of Italian descent, noted intermittent sharp pain originating in the left fifth finger for six years before the first clinic admission in 1944. The pain occurred only when the finger was bumped or struck, although there was always a small tender area on the medial, terminal aspect of the fifth finger. It was from this site that the pain originated and radiated upward into the arm in a sharp lancinating fashion. Past history was otherwise uneventful except that she had undergone hysterectomy for leiomyomas in 1939.

General physical examination revealed nothing unusual except the tender area described, pressure on which consistently reproduced the usual radiating disturbance. This symptom could be elicited as often as the trigger area was stimulated. There was no evidence of swelling, tumor, or infection. The first roentgenograms, taken Aug. 23, 1946, showed an area of bone destruction in the base of the fifth left distal phalanx, with distortion of the cortical bone on the thenar side (Fig. 1, *B* and *C*). There was slight swelling of the adjacent soft tissues but no evidence of joint involvement or radiopaque foreign body. The roentgenologist suggested the possibility of a bone infection.

Although a glomus tumor was suspected clinically, nothing further was done because the patient, being relatively symptom-free, refused surgery. She was seen periodically, and x-ray views on Oct. 25, 1946, showed little if any change in the appearance of diminished density. The roentgenologist "doubted the existence of an osteomyelitis, but favored the likelihood of some sort of cystic disease." He was still unaware of the clinical aspects of the case. Because of persistence of the symptoms which were apparently more annoying than severe, the patient again returned, but x-ray views on Jan. 31, 1947, revealed no appreciable change. With a bright light, the radiologist noted a faint shadow distal to the break in the cortex, which suggested that some of the material had escaped from the cystic area, although there was no apparent change in the contour of the external margin of the soft tissue. The lesion was called a cyst although the doubtful possibility of an enchondroma was considered.

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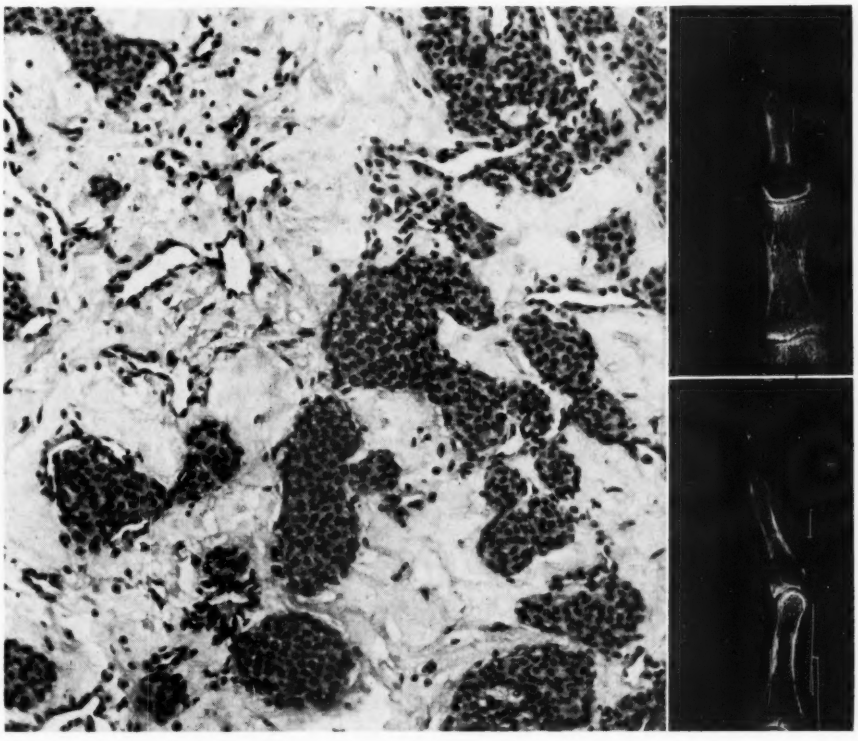
*Now Director of Laboratories at Good Samaritan Hospital, Portland, Ore.

On Feb. 7, 1947, the finger was explored under local finger block. An oval incision was made, laying back the anterior closed space. A soft pink tumor mass 4 mm. in diameter was found within the phalanx at its base, protruding mesially into the soft tissue through a small break in the cortex. The tumor was removed by dissection and thorough curettage, and the skin flap sutured with interrupted silk.

In November, 1947, the patient complained of some tenderness only when the scar was touched in the proximal portion. No pain was present. An x-ray picture was taken which showed beginning regeneration of bone in the phalanx previously occupied by the tumor.



A. *B.* *C.*

Fig. 1 (Case 1).—*A*, High-power photomicrograph showing typical glomus tumor; *B*, anteroposterior view of terminal phalanx revealing punched-out cystic space in the proximal end; *C*, lateral view of same phalanx.

Tenderness in the scar persisted and it was excised under local anesthesia on March 13, 1948. Section showed only cicatricial tissue. The wound has healed well and the patient had no symptoms when last seen on March 27, 1948.

The photomicrograph, Fig. 1, *A*, shows the typical picture of a glomus tumor composed of clear, round to oval cells, surrounding in an organoid fashion the endothelial-lined spaces. Bodian's stain showed moderate numbers of neurofibrils in the stroma between the cellular islands.

Case 2.*—L. K., a 36-year-old housewife of Polish descent, was admitted to Bellevue Hospital in September, 1946, complaining that her thumb had hurt for ten months. Two years previously, she had injured the right thumb wedging it between two cement buckets while working in a shipyard. There was no excruciating pain at the time, but fourteen months later she noted the gradual onset of lightning-like pains originating in the thumb

*Grateful acknowledgment is given to Dr. Gordon Lee, Chief Surgeon 1st Surgical Division, Bellevue Hospital for permission to publish this case.

immediately mesial to the nail and radiating into the arm in a sharp shooting fashion. The pain was initiated by changes in weather and temperature or slight pressure on an area adjacent to the nail. The pain became progressively more severe and frequent, the trigger mechanism apparently becoming more and more sensitive. One month prior to admission, the patient underwent a series of x-ray treatments, but the amount and technical approach was unknown. These gave no relief.

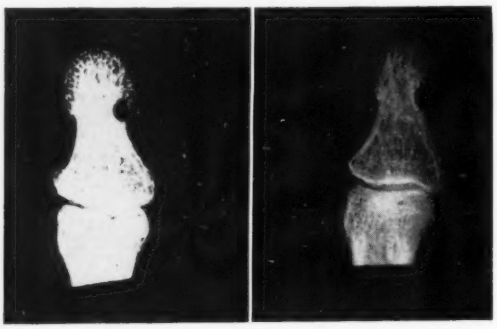


Fig. 2 (Case 2).—Identical anteroposterior films of different intensities disclosing circumscribed radiolucent area completely surrounded by bone.

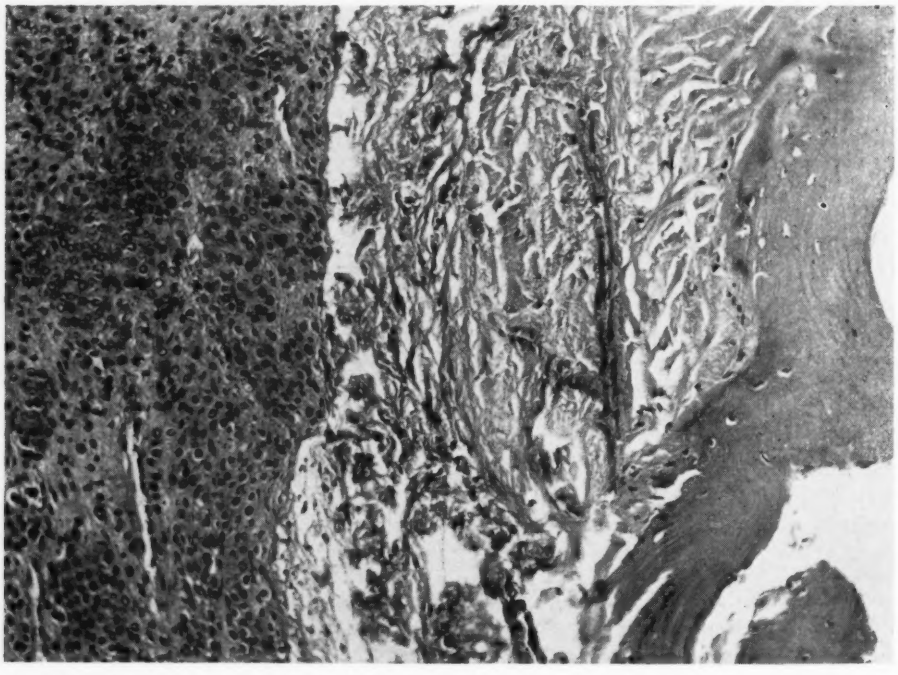


Fig. 3 (Case 2).—Photomicrograph showing glomus tumor and encompassing bone curetted from lesion seen in Fig. 2.

Several months after x-ray treatments, she had a tan, discolored, smooth, though slightly scaly thumb, without swelling or inflammation. Directly mesial to the thumbnail, there was a small 2 mm. area of pinkish discoloration with an adjacent 2 mm. area firmer than the surrounding tissue. These formed the center of a 6 mm. area, acutely tender to the slightest touch, and together composed the trigger region which set off the agonizing pain radiating into the arm. The remainder of the physical examination and the past history contributed nothing pertinent to this condition.

Anteroposterior x-ray views of the phalanx, Fig. 2, showed a cystlike structure on the mesial border. The overexposed film on the left discloses a very small break in the overlying cortex. Glomus tumor was not considered by the radiologist.

A 1.5 cm. linear incision, 0.5 cm. inferior to the radial border of the nail, was made under brachial nerve block supplemented by nitrous oxide inhalation. The incision revealed a round cystic structure, 3 mm. diameter, in the radial aspect of the terminal tuft of the distal phalanx. The cyst was occupied by a firm nodule of tissue, somewhat pinker than the adjacent soft tissue. The overlying bone was soft, thin, and disrupted. The mass was excised and the cyst curetted. The wound, closed with interrupted silk sutures, healed per primam.

The photomicrograph, Fig. 3, shows bits of cancellous bone adjacent to masses of epitheloid cells completely surrounding endothelial-lined spaces. Bodian stained sections reveal moderate numbers of neurofibrils in the fibrous stroma.

To date, April 1, 1948, the patient has been completely relieved of symptoms.

DISCUSSION

In the past thirty-seven years, fifty-two cases of glomus tumor were diagnosed in The Surgical Pathology Laboratory at the College of Physicians and Surgeons. Twenty-six were found on the fingers and of these, fifteen were subungual. In only two additional cases, both subungual, were they found on the toes. The remaining cases were distributed over other regions of the body, involving the eyelid, arms, elbows, forearms, wrist, thigh, knee, and ankle. Of this latter group, the majority occurred in the forearm and knee. It is noteworthy that phalangeal glomuses develop predominately in females, while in males they occur chiefly elsewhere. That the glomus tumor is not limited to the fingers is further brought out by these cases developing in bone and another very unusual glomus tumor, histologically typical, found in the wall of the stomach.

The origin and development of these neoplasms in areas remote from the normal glomus at the cutaneous-subcutaneous junction are controversial and intriguing. Stout and Murray,[4] growing explants of glomus tumors by tissue culture technique, came to the conclusion that the glomus epithelioid cell is identifiable as the pericyte described by Zimmermann. They offered this hypothesis to explain the occurrence of glomus tumors in those regions of the body where no normal glomuses are known to exist.

SUMMARY

Two cases of glomus tumor, each enclosed within the bone of the terminal phalanges of the fingers, are reported. Both were curetted, providing immediate relief. Neither case was diagnosed by roentgenologists who were unaware of the clinical findings. Almost one-half of the glomus tumors occur in regions other than fingers and toes.

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Case Reports

PRIMARY SPINDLE-CELL SARCOMA IN A MECKEL'S DIVERTICULUM

FRANK T. MCGINNIS, M.D., PHILADELPHIA, PA.

(From the Misericordia Hospital)

SINCE 1812, when Meckel[11] first described the anomalous diverticulum of the ileum, which bears his name, this structure has been calculated by various authors to occur in from 1 to 3 per cent of the population. Malignancy in the small bowel is extremely rare, comprising approximately 2.5 per cent of all gastrointestinal malignancies, while only 0.1 per cent of these are found in the ileum proper.[16] Moses,[13] in a collective review of 1,605 cases of Meckel's diverticulum, found that malignant changes occurred in 1.5 per cent, or twenty-four cases. A careful search of the literature reveals only four previously reported cases of primary spindle-cell sarcoma in a Meckel's diverticulum. The following is submitted as a fifth case.

CASE REPORT

D. O'B., a white man of about 60 years of age, was admitted to surgical service under my care on Sept. 1, 1947, complaining of abdominal pain, vomiting, and diarrhea of one day's duration. The vomitus had consisted of undigested food. There was no hematemesis. Frequent loose, black bowel movements containing some bright red blood had occurred during the preceding twenty-four hours. In the seven months prior to admission there had been thirty pounds weight loss, frequent attacks of colicky lower abdominal pain, and tarry stools. On admission the pain was described as severe, sharp, and localized to the right lower quadrant.

Temperature on admission was 100° F., pulse 104, respirations 20; hemoglobin 11 Gm. (70 per cent); red blood count 3.60, and the white blood count 13,400. The urine analysis was essentially negative. The patient appeared pale, anxious, and restless. On deep palpation tenderness was present in the right lower quadrant and suprapubically. There was a suggestion of rigidity in the latter area. An irregular, tender mass was palpable between the umbilicus and the pubis. The impression following examination was Meckel's diverticulum.

The patient had had one other admission to this hospital, in December, 1942. At that time he was complaining of weakness, nausea, and vomiting and gave a history of tarry stools which had also occurred once, six months previously. Gastrointestinal studies at that time showed atrophic gastritis. The blood picture was that of a normochromic normocytic anemia. Several blood transfusions together with iron and liver therapy were given and the patient was discharged to the care of his family physician.

Since there was every indication that the patient presented an acute condition of the abdomen at this time, an emergency laparotomy was decided upon. Using spinal anesthesia the abdomen was opened through a lower midline incision. A cauliflower-like mass about six inches in diameter, containing a small perforation which was leaking, was adherent to the anterior abdominal wall. The adherent portion was necrotic and friable

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and dissected with difficulty. Upon delivering the mass, inspection revealed it to be located on an outpouching of the ileum approximately eighteen inches from the ileocecal valve. The mass, together with about eight inches of ileum, was resected and a side-to-side anastomosis was done. An enterostomy tube was inserted in the small bowel proximal to the anastomosis. At the beginning of the operation the patient's blood pressure was 82/60. He then lapsed into profound shock, later rallied, and at the close of the operation the blood pressure was 52/30. Intravenous fluids were given throughout operation.

Postoperatively, blood and plasma transfusions were administered as well as intravenous glucose. A Miller-Abbott tube was passed and Wangensteen suction set up. The accepted doses of penicillin and streptomycin were given.

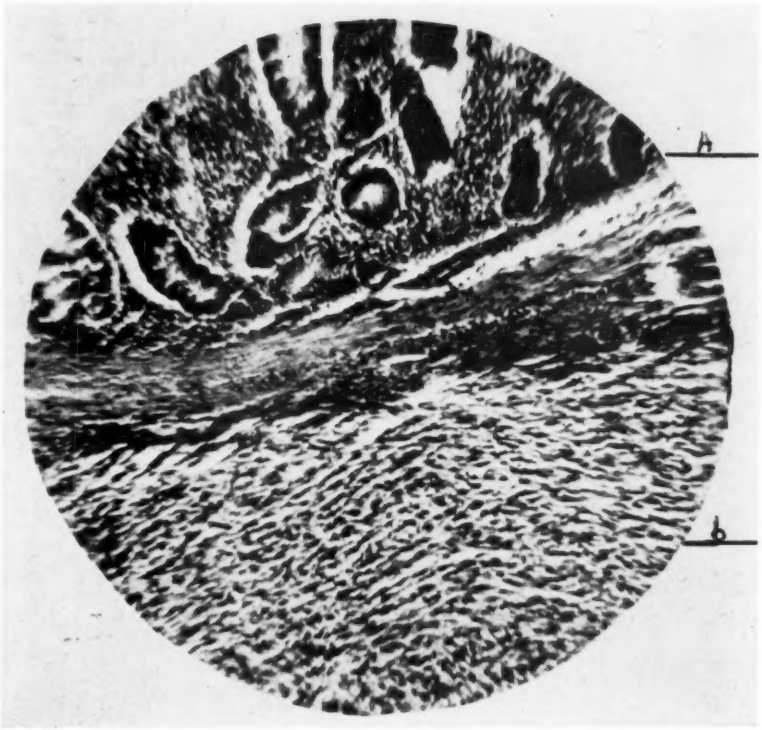

Fig. 1.—Photomicrograph showing section taken from edge of orifice of diverticulum. *a*, Ileal mucosa and subjacent tissue; *b*, tumor (spindle-cell sarcoma) infiltrating tissue. (Magnification ×90.)

Thirty-six hours after operation the patient again went into shock, the blood pressure dropped, temperature continued to rise, and the abdomen became distended. He died about sixty hours postoperatively. An autopsy was not obtained but, clinically, peritonitis with peripheral vascular collapse appeared to be the cause of death.

The following pathologic report was submitted.*

Gross Description.—A specimen consisting of a pinkish injected glistening, puckered, globular mass of tissue 11.5 cm. in diameter was received in moist gauze. There was a small perforation 2 mm. in diameter on one side. A smooth and glistening tubular structure, 1.5 cm. in diameter, which was apparently small intestine with a narrow band of attached mesentery, traversed the mass on one aspect. This also protruded for about 6 cm. on either side of the mass. Upon opening the specimen it was seen that the mass was antimesenteric in its position and was part of an outpouching of the intestine. The wall was comprised of a

*By our pathologist, Dr. Emmet F. Ciccone.

fleshy white material which cut with moderate resistance and varied from 2.0 to 3.5 cm. in thickness. The inner aspect presented a ragged friable hemorrhagic appearance. The opening into the intestine was 1.5 cm. in diameter.

Microscopic Examination.—Examination of the edge of the area from which the tumor was taken showed it to be ileum. The mucosa was intact and the lymphoid follicles could

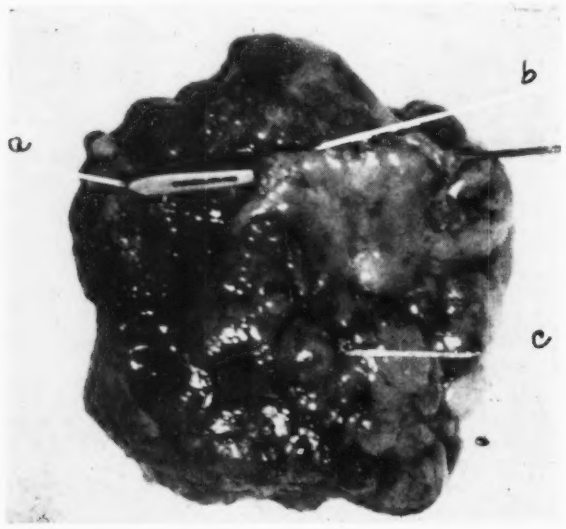

Fig. 2.—Photograph of gross specimen showing *a*, probe through ileum; *b*, mesenteric border of ileum; c, sarcomatous mass in the wall of Meckel's diverticulum.

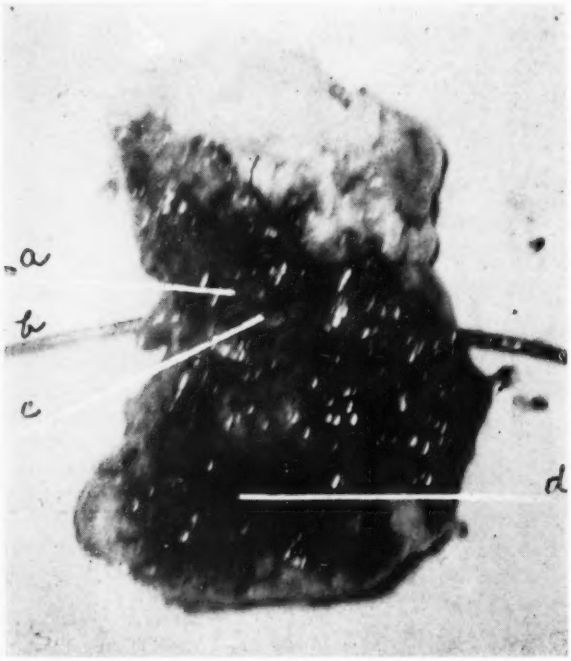

Fig. 3.—Photograph of tumor mass opened in the axis parallel with ileum. *a*, Orifice of diverticulum; *b*, probe in ileum which can be seen through orifice of diverticulum at *c*; *d*, inner surface of mass showing hemorrhage and necrosis.

be visualized. Adjacent to this, destroying and infiltrating the tissue, was a very highly anaplastic connective tissue type of tumor consisting of cells arranged in bundles coursing in various directions. The individual cells were relatively large and spindle shaped and had large hyperchromatic nuclei. The nuclei were granular in areas and contained mitotic figures. Much necrosis was noted together with infection.

Diagnosis.—The diagnosis was spindle-cell sarcoma originating in the wall of a Meckel's diverticulum.

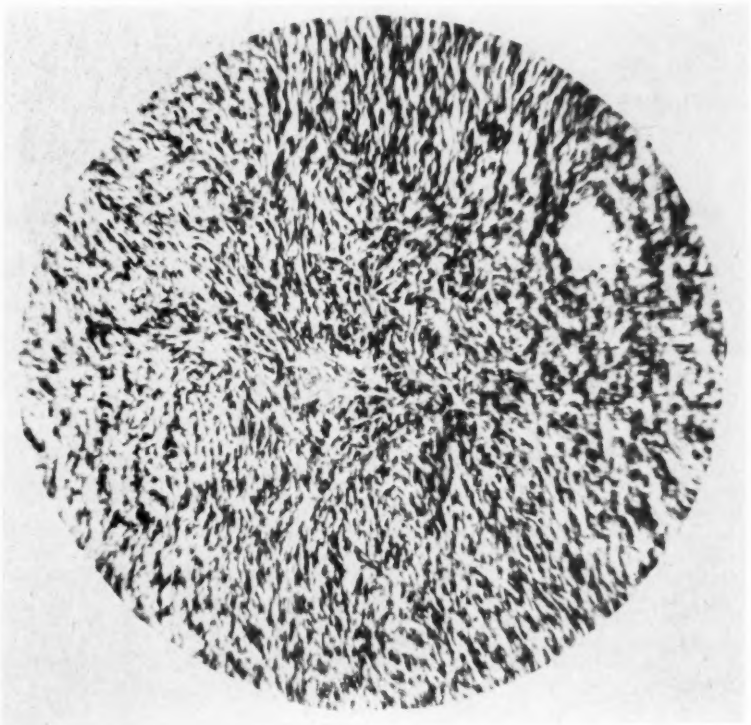

Fig. 4.—Another photomicrograph showing tumor proper. (Magnification ×90.)

The exact incidence of pathologic changes in Meckel's diverticuli presenting clinical evidence of disease has never been accurately determined. The most common complications encountered, in the order of frequency, are hemorrhage, intestinal obstruction, perforation, Littre's hernia, and simple diverticulitis.[13]

Of the twenty-four reported cases[13] of malignancy, four were spindle-cell sarcomas,[3, 8, 9, 17] seven carcinomas,[1, 2, 12] and thirteen sarcomas of various types.[6, 10, 13, 14, 15]

The first case of spindle-cell sarcoma was reported by Kaufman[9] in 1911. He merely stated that in the Basel collection there existed a case of spindle-cell sarcoma in a Meckel's diverticulum. The specimen was about the size of a hen's egg and occurred in a woman 72 years of age. There was no further description of the tumor or the case history of the patient. Tschinknowerow[17] in 1911 and Haessner[8] in 1913 each reported a case of spindle-cell sarcoma originating in a Meckel's diverticulum. Tschinknowerow's case was found at autopsy in a woman 62 years of age. Haessner's patient was a 50-year-old man who died

postoperatively. The case history of this patient is similar in many respects to the patient under discussion—the history, presenting symptoms, and death occurring in much the same manner. In 1925, Crile[3] successfully removed a Meckel's diverticulum containing a primary spindle-cell sarcoma from a 41-year-old woman. This patient was given a course of deep x-ray therapy and was in apparent good health one year postoperatively.

SUMMARY

A fifth case of primary spindle-cell sarcoma originating in the wall of a Meckel's diverticulum is herewith submitted, together with a brief review of the four previously reported cases.

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LUNG HERNIA

A Case Report

LAWRENCE S. MANN, M.S., M.D., KENNETH C. OLSON, M.D.,
AND WALTER S. WALLS, M.D., BATAVIA, N. Y.

(From the Department of Surgery University of Buffalo School of Medicine and the Surgical Service, Veterans Hospital)

WE SHALL not attempt to review the literature on lung hernia in this paper as this has been recently accomplished by Maurer and Blades.[1] Hernia of the lung is generally classified into three types:[2] congenital, spontaneous, and traumatic. Since Roland[3] reported the first case of lung hernia, less than 200 have been reported. We are presenting this case of a 49-year-old boxmaker, who acquired a lung hernia following fracture of the ribs. The lesion falls into the classification of the traumatic type, which is most common.

CASE REPORT

R. W. K., a 49-year-old boxmaker, on arrival at Batavia Veterans Hospital on March 20, 1947, complained of frequent coughing spells and pain on the left side of the chest. He also has coughed up small amounts of blood on occasion in the morning. A bulge was present on the left side of the chest, which reached maximum size on forced expiration or coughing, and was practically not visible on quiet breathing or inspiration. When the bulge was prominent, pain in this area was increased by coughing.

The patient stated that he was entirely well until about June 6, 1945. He was stationed in Germany at that time. One day, while walking, he tripped, falling over a piece of rope which was strung across the road. He had considerable pain on the left side of the chest. He reported to the dispensary where a diagnosis of fractured ribs on the left side was made. At a general hospital in Germany, the patient was given a nerve block for relief of the pain. He was evacuated to the United States and subsequently discharged from the Army. Shortly before discharge, he noticed a small bulge on the left side of the chest which occurred on deep expiration or coughing. He then went to work in a carton factory and could work only for a few days at a time because of persistent coughing spells, which would cause considerable pain in the left side of the chest over the area of the bulge. In the morning he occasionally coughed up small amounts of clotted blood, about the size of a marble. The past history was irrelevant.

The physical examination was not remarkable except for a bulge about the size of a lemon between the fifth and sixth ribs on the left, extending from the anterior axillary line to the midclavicular line. The bulge appeared during expiration and disappeared on inspiration. The mass protruded best on coughing and forced expiration with the Valsalva maneuver (Figs. 1 and 2). On palpation the bulge was felt to be a soft crepitant mass. There was a definite defect in the interspace. The patient complained of pain in the region of the hernia when it protruded and had relief of pain when the hernia was reduced. Vocal and tactile fremitus were increased and vesicular breath sounds were heard over the hernia.

X-ray examination of the chest revealed healed fractures of the left fourth and fifth ribs anteriorly. Roentgenograms made while the patient was performing Valsalva's maneuver showed that the lung herniated outside of the thoracic cage (Figs. 3 and 4).

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Preoperatively, an artificial pneumothorax was performed followed by fluoroscopy and x-ray examination, which demonstrated the lung to be adherent to the pleura. The patient received the usual preoperative preparation.

Operative Procedure.—On April 8, 1947, the anesthesia was induced with intravenous sodium pentothal and switched over to endotracheal nitrous oxide, oxygen, and ether. An incision was made between the fifth and sixth ribs, extending from the midaxillary line forward about six inches. The incision was carried down through the serratus anterior muscle. In this region, the intercostal muscles appeared thin and somewhat atrophic. The pleural sac was opened. The lung was not adherent to the sac, but was adherent to the pleura along the inner surface of the sixth rib. The lung was freed from the pleura. The pleura was closed with interrupted silk sutures. The intercostal muscles and serratus anterior were approximated over the pleura. A periosteal flap about two and one-half inches in length was turned down from the fifth rib and a similar flap was turned up from the sixth rib. The free borders of the periosteal flaps were then sutured together with interrupted silk sutures over the previous layer of muscle closure. The superficial fascia and skin were closed in layers with interrupted silk sutures. All the air was not removed from the left pleural cavity when the pleura was closed, leaving a partial pneumothorax.

Fig. 1. Fig. 2.

Fig. 1.—Chest wall during forced expiration (Valsalva maneuver).
Fig. 2.—Chest wall during inspiration.

Postoperative Course.—Postoperatively, the patient received 50,000 units of penicillin, intramuscularly, every three hours for a few days. He was completely ambulatory the first postoperative day. Sutures were removed on the seventh postoperative day. The wound healed per primam. The postoperative course was entirely uneventful.

An x-ray view taken one week postoperatively showed a fairly large pneumothorax with a small amount of fluid at the base. The mediastinum was displaced to the right (Fig. 5, *A*). Two weeks after surgery, the chest showed no evidence of free fluid. The mediastinum was not displaced (Fig. 5, *B*). Figs. 6 and 7 show the chest wall two weeks postoperatively during forced expiration and during inspiration.

Fig. 4.—Roentgenogram during the Valsalva maneuver.

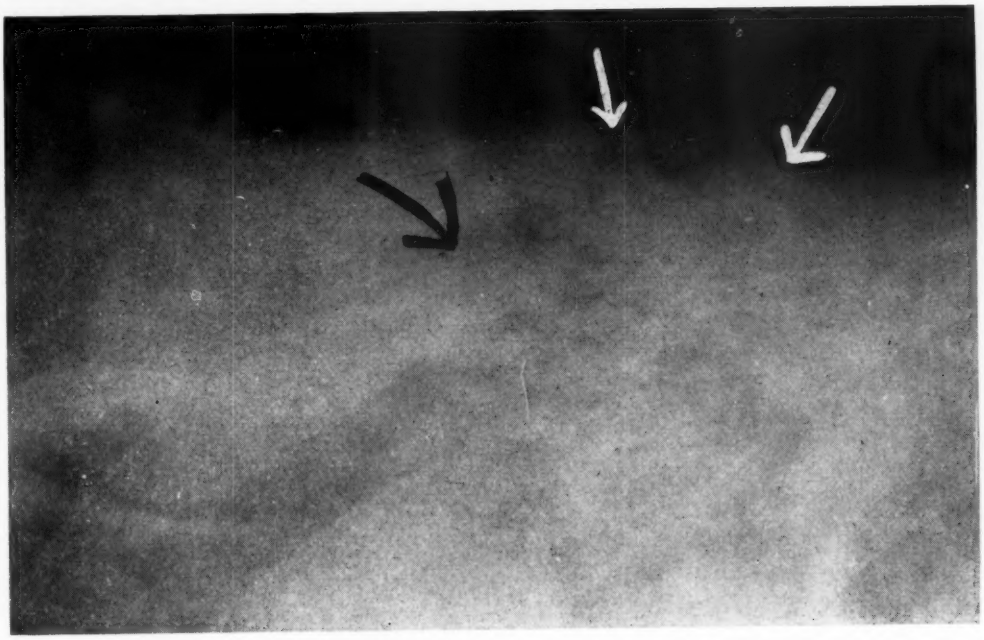
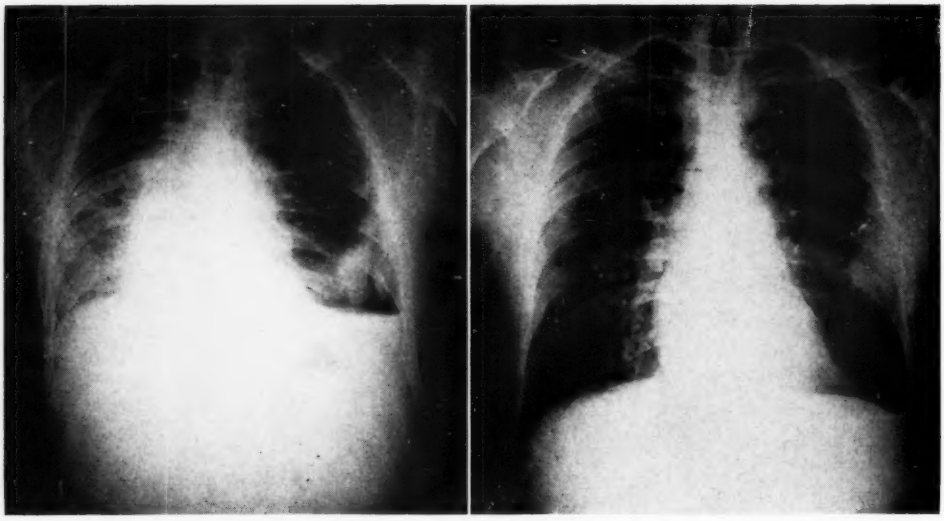


Fig. 3.—Roentgenogram during the Valsalva maneuver.



A. *B.*

Fig. 5.—*A*, Left, x-ray taken one week postoperatively showing pneumothorax; *B*, right, x-ray taken two weeks postoperatively, lung has re-expanded and fluid in left chest has disappeared almost in entirety.

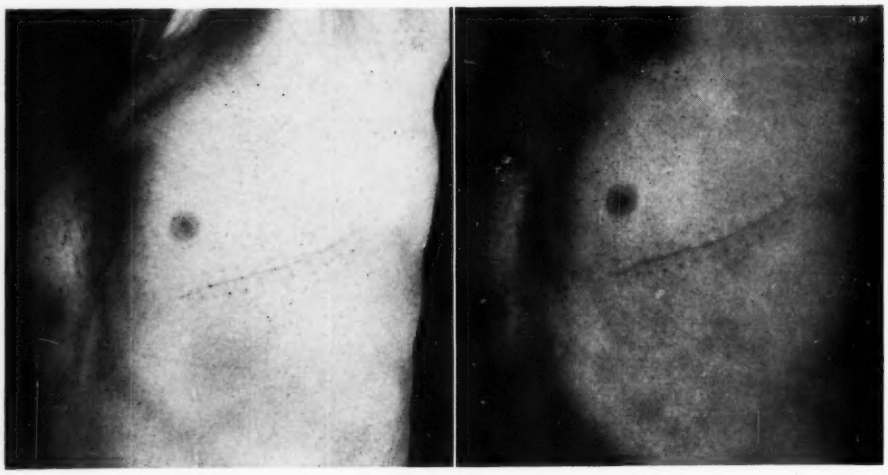


Fig. 6. Fig. 7.

Fig. 6.—Chest wall, two weeks postoperatively, during forced expiration.
Fig. 7.—Chest wall, two weeks postoperatively, during inspiration.

DISCUSSION

This patient presented typical signs and symptoms of lung hernia. The diagnosis was made on the history and physical examination, confirmed by x-ray examination. The patient gave a history of injury to the thoracic cage in which some ribs were fractured about twenty-one months prior to admission. A few months later he developed a bulge between the fifth and sixth ribs on the left anterolateral side of chest wall. According to Schwartz[4] this is the most common location because the intercostal spaces are very wide in this region. The physical

examination revealed a soft, boggy, crepitant mass coming through a defect in the interspace between the fifth and sixth ribs. This mass reached a maximum during forced expiration and diminished in size during inspiration or quiet breathing. Pain was associated with the bulge. Vocal and tactile fremitus were increased over the hernia. Vesicular breath sounds were also heard.

The operative procedure, performed under endotracheal anesthesia, was similar to that used by Maurer and Blades.[1] The lung was freed from the pleura, in order that it would not continue to press against the defect. The intercostal muscles were atrophied. Korol[5] mentioned this finding in his cases. We employed the technique of Goodman[6] in developing periosteal flaps from the ribs above and below the defect and then suturing these flaps together over the defect. Bone will eventually form over the defect and this will give added support to the chest wall.

No attempt was made to correct the resultant pneumothorax because we wished the air to act as a buttress or cushion between the lung and repaired defect.[1]

The patient was completely ambulatory and comfortable the first postoperative day. Codeine was used to suppress coughing. Penicillin was given as a prophylactic against infection. The postoperative course was entirely uneventful.

SUMMARY

1. A case of lung hernia is presented.
2. Techniques previously developed have been utilized in the surgical repair.

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Editorial

Medical Service in the Armed Forces

IT WAS Napoleon who stated that an Army was no better than its doctors, and this has remained true over the ensuing years. In time of war our services have had available an ample number of highly specialized medical officers. They have not always been assigned wisely, for specialists have been used to perform duties which could be performed by men with lesser training and experience. Medical officers are still being made to sit on boards which do not require their services, to sign for property which they do not really control, and to do a host of other duties which in effect wastes their time. Slowly, but surely, medical officers are being relieved of these tasks, and assignments are being made with more regard to an officer's training and experience. These changes must be made to an even greater extent than they have been, for we can no longer afford to squander medical personnel.

The present peacetime authorization of increase in size of our armed forces will require a major augumentation of medical personnel. It is not enough that young doctors recently out of internship shall become available for active duty. The armed forces will require men who have been trained in the various specialties if the augmented forces are to obtain the type of professional care which mothers and fathers have a right to expect.

It may be interesting historically to review the ideas of a great field commander—one who in his later life defeated Napoleon at the Battle of Waterloo—the Duke of Wellington. On July 1, 1797, Colonel Wesley, who later became the Duke of Wellington, wrote to Baron Teignmouth, then the Governor General of India, as follows:*

> Sir
>
> I have been informed that the medical Board have received a letter from the Secretary of the Supreme Board stating it to be the resolution of the Governor General in Council that the usual allowance of S^{r} Rupees 2. .8 per month for each of the European troops embarked on the Intended expedition be granted to the Surgeons of the Indiamen on which they shall embark—As I heard some days ago that there was a doubt upon this subject I did myself the Honor of waiting upon you yesterday & the day before have some conversation with you upon it; but unfortunately you was not well; & I should now wait upon you again only that I fear you are not recovered, & I imagine it will be more satisfactory to you to have my sentiments in writing than in conversation—I have to state to you that this arrangement is inconsistent with the principles of the former practice even in voyages from England to India, that it will not tend to the preservation of the health of the men, that it takes out of my hands entirely the Superintendence & control over the management of the Sick, & that it will be extremely injurious to the Surgeon of the 33^{d} reg^{t}—

*I believe this letter has not hitherto been published.

I hope to be able to convince you of the truth of these propositions: & if I do I am certain that you will wish to have this subject reconsidered by the Board, & that the arrangement will be altered—

I am willing to admit that when the King's or Company's recruits are embarked on board an Indiaman & brought from England it has been usual to pay the Surgeon half a Guinea per man, upon the certificate of the military Commanding Officer, or of the Commander of the Ship if there is no military Commanding Officer that he has attended them during their voyage—The certificate of the Commanding Officer is the proof required of the attendance, but now such certificate even where there is a whole regt concerned is not required: not only they may not attend the Sick, but they may neglect to provide what is necessary for them and yet they will be entitled to their allowance—

If a regt is embarked on board an Indiaman coming from England I conceive that if the Commanding Officer chuses to refuse to employ the Surgeon of the Ship he is at liberty so to do: & he may afterwards if he pleases decline to give him the certificate of attendance & he may give it to his regt Surgeon—The former I have always practiced, the latter I have refrained from, because I have not wished to be the cause of disappointment to any body—This certificate however would entitle the regimental Surgeon, even upon a voyage from England, to the allowance given by the Company for medical attendance upon the troops during such voyage—But it appears that this is a military expedition, & not a common voyage of transport from place to place; & therefore in this above all other voyages, care should be taken that the Sick are properly attended, & that allowances are not paid where proper provision for them has not been made—

If the troops were embarked in common transports or in ships unprovided with Surgeons, this same medical allowance would be given to the Regt Surgeon; where then is the difference in this case? what can be the advantage of taking the Sick from under the care of their own Surgeons? They will be placed under that of persons totally unaccustomed to them & who even if they were the first men of their profession would labor under that disadvantage, which is fatal in so many instances—Besides the certificate of attendance from the Commanding Officer being no longer necessary attendance may not be given & allowances will still be received—

These Gentlemen being under the orders of their own Officers they may & they ought to refuse to have any communication with me upon the subject of the Stores medicines &c &c with which they supply their ships; They will refuse to obey any orders or regulations of mine in the detail of the management of the Hospitals; They will refuse to give me or my Officers even the Common Sick Reports (of which I have known instances even in the voyage from England) & thus I shall be deprived of that part of the Superintendence over my Corps which is most gratifying to me when they are embarked & by exercising which I can render most Service to the Soldiers—This considering the claims

of command which have been already made, will be exceedingly disagreeable & distressing to me—

It will not be denied that this arrangement is very disadvantageous to the Surgeon of the 33[d]; to whose attention to his duty, & whose exertions I am indebted for the lives of many men both before and since my arrival in this country—But I must inform you Sir that not only it deprives him of a fair emolument but it confers it upon a set of men, who if my information respecting the practice upon this subject be correct, have done that for which they ought to be dismissed their Service instead of being rewarded.—

The proposal of the medical Board I understand was that S[r] Rupees 2. .8 per month for each man should be given to the Regimental Surgeon to find medicines, wine &c &c; and that in those ships in which there should be no Surgeon of the 33[d] embarked, the allowance of the Surgeon of such ship should be one Rupee per month for each man in case they were furnished with medicine—If this subject is reconsidered, & the arrangement is altered, the Surgeon of the 33[d] is willing to furnish those ships with all the necessary medicines, wine, attendance of Servt[s] &c &c, & to make the allowance of one Rupee to the Ship Surgeons who give their attendance as proposed by the medical Board; or to agree to such other arrangement as you or the Medical Board may think fit to propose—

I have the Honor to enclose a copy of the arrangements which have been made upon this subject at Madras—You will observe that the regimental Surgeons upon that establishment receive this allowance for the attendance of Servants upon the Hospital, & food for the sick &c &c only, & that medicines of all kinds, & wine are provided for them: but the Surgeons of 33[d] will be content with what has been proposed to be given to the Surgeons of the Indiamen, & I trust that considering what I have above stated, & the Hardship & disgrace under which he will labour of serving in the same army with Surgeons of another establishment, who will have all the charge of the hospitals & double his allowances & emoluments, as the Surgeons of the Indiamen will have the charge of his Hospital you will be induced to have the subject reconsidered—

I have the Honor to be Sir
Your most obedient H[ble] Serv[t]
A. Wesley

Social structure and our economy have changed considerably in the 151 years since Colonel Wesley wrote this letter. The professional needs of the armed forces in peace or in war have not become less but have become greater. It is to be hoped that the medical profession, and surgeons in particular, will realize this and will provide every help to the end that the men who are to become a part of the peacetime draft forces will be provided the medical and surgical care which they have every right to expect.

—I. S. Ravdin

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

PORTAL HYPERTENSION

WITH SPECIAL REFERENCE TO THE ACID-PEPTIC FACTOR IN THE CAUSATION OF HEMORRHAGE AND EXTENSIVE GASTRIC RESECTION IN ITS TREATMENT

IVAN D. BARONOFSKY, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

INTRODUCTION

General Considerations

WITH the steady decline of surgical mortality rates during the last ten years, there has been a more aggressive attack on pathologic states that have heretofore been considered fatal. The improvement in diagnostic measures, preoperative and postoperative care, anesthesia, and the advent of the antibiotics and chemotherapy have been partly responsible in this decline. However, of more importance is the realization that the preparation of the surgeon with attention to meticulous technique, and a disregard of time, makes for an uncomplicated procedure and an uncomplicated recovery. The decline of mortality associated with gastric resection is evidence of these facts.

The purpose of this paper is to present a study of the surgical therapeusis of bleeding from esophageal varices in conditions which give rise to portal hypertension. A consideration relating to elimination of the stomach as a mode of treatment of the bleeding associated with portal hypertension will be made.

REVIEW OF THE LITERATURE

Anatomy of the Portal System

Anatomy of Veins of Portal System.—The portal vein receives the venous drainage of the stomach through the left gastric vein, and thence passes into the free border of the gastrohepatic ligament, where it lies behind and between the common bile duct and the hepatic artery and passes into the liver at the hilus. The portal vein is formed by the fusion of the superior mesenteric and the splenic veins, which drain the small intestine and right half of the large bowel, and the spleen, respectively. The splenic vein also receives the inferior mesenteric vein which ascends obliquely toward the right and forms the left border of the duodenojejunal fossa and then passes behind the root of the transverse mesocolon and the pancreas. The purpose of this portal system is to sidetrack to the liver

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the venous return flow from the great splanchnic area of the intestine which is rich in absorbed foodstuffs.

It might appear that this brief description of the normal or typical arrangement is sufficient; however, there are variations which though rarely described as a group are nevertheless very important when the symptomatology of portal hypertension is to be assessed. Thus Rousselot (1940) portrayed six different anatomic patterns taken from six standard sources. This fact is rightly stressed and poor results after certain surgical procedures may have their explanation here.

The venous drainage of the lower end of the esophagus is not considered adequately in many textbooks. Preble (1900), in a review of sixty cases of fatal gastrointestinal bleeding due to cirrhosis of the liver, stated that the anastomosing branches at the cardioesophageal junction were too small or too few to contribute much to the formation of a collateral circulation when the portal system is obstructed. When the anastomosis is free, they may become an important factor and then dilatation may so completely compensate for the veins obstructed in the liver that the clinical course of the cirrhosis is often altered and obscured. Preble believed that free anastomoses were exceptional and this circumstance, he believed, explains why varices are not always found in the lower esophagus in instances of portal hypertension.

Kegaries (1934), in an excellent study, described the anatomy of the veins of the upper end of the stomach and the lower end of the esophagus. He injected the left gastric vein and then cleared the specimens. Of the sixteen cases that were judged to be accurately and satisfactorily injected, only eight revealed evidences of anastomotic circulation sufficient for further study. It is stated that the failure to obtain satisfactory injection cannot be ascribed to the inherent lack of anastomotic channels although such a condition must be recognized.

The failure to demonstrate definite venous dilatations or bleeding points at post-mortem examination of patients dying of hemorrhage due to portal hypertension is ascribed by Bell (1944) to collapse of the veins at death. Yet it may be entirely possible that even if injection studies were made, no dilated esophageal veins would be found. Kegaries (1934) found the submucosa of the esophagus to be richly supplied with veins situated both above and below the muscularis interna, the former lying quite close to the mucosa or protective layer. A fine anastomosis between the canal and portal circulation was shown to exist at the extreme lower end of the esophagus. Textbooks of anatomy (Gray, 1942, Cunningham, 1926) consider that the esophageal veins in general drain into the caval system, while those from the stomach drain into the portal. The arterial supply of the abdominal portion of the esophagus is obtained by way of the left gastric artery, the inferior phrenic artery, and numerous anastomoses between vessels of the abdominal and thoracic portions of the esophagus. The venous drainage of the abdominal esophagus is similar (Demel, 1924).

The cardia of the esophagus was considered by Kegaries (1934) as the lower 4 to 5 cm. and in this region the fine anastomoses run longitudinally with an absence of cross anastomoses. Occasionally two or three larger veins were found to be crossing the cardia. Tosetti (1916), on post-mortem examination of three

cases of "phlebectasia" of the esophagus, had seen three enlarged trunks plus a flat ulcer of the cardia. It is important to note that histologic study of the cardia reveals that it is strongly supported by loose connective tissue and the mucosa was also more adherent in this region and was bound together by interlacing elastic fibers and connective tissue.

Vascular Anatomy of Hepatic Lobule.—The human liver is made up of small polygonal lobules which appear as yellowish-brown circumscribed areas of about 0.5 to 2 mm. in diameter. Running through the center of the lobule in its long axis is the central vein. At the periphery of each lobule are prolongations of the capsule of the liver (Glisson's capsule) in which are the hepatic ducts, the portal veins, the hepatic arteries, lymphatics, and nerves which Kiernan (1833) called the portal canals.

In each of the lobules blood may enter by way of numerous portal vein branches but empties by only one central vein. Eppinger (1937) has made the claim that in certain instances where the central vein fails to drain adequately one may obtain an overfilling of the liver. The central veins unite to form sublobular veins and these in turn empty into collecting vessels and these then end in the hepatic veins.

Deysach (1941), in an interesting series of experiments, showed the presence of "sluice channels" in the liver of the rabbit, cat, and monkey. These "sluice channels" are small endothelial tubes which arise from the confluence of many ordinary sinusoidal capillaries. These channels drain directly into the sublobular veins. The size of the lumina varies greatly, which suggests to him that the channels probably open and close passively as the sublobular veins dilate and constrict. These observations present a mechanism of regulating the flow of blood through the liver.

There is a great difference of opinion as to where and how the blood from branches of the hepatic artery and that of the portal vein mix. That there is some form of communication everyone seems to agree. Mall (1906), and later Gilbert and Villaret (1909), came to the conclusion that there was a direct union of the branches of the portal vein and hepatic artery in the interlobar spaces. However, it must be stated that these were injection studies and complete visualization was not obtained. Olds and Stafford (1930), with a much improved method, postulated that the mode of distribution of the hepatic artery blood is by small branches of the hepatic artery passing directly into the liver sinusoids.

Wakim and Mann (1942) accepted the presence of anastomoses between the arterial and portal radicals in their course through the interlobular spaces. Herrick (1907) perfused normal and cirrhotic livers through the hepatic artery and portal vein and noted the effect of one on the other at increasing pressures. He pointed out that in the normal liver two circulations were present with reciprocal volumes and pressures which were contained in a freely expansible tissue framework. The equalization of pressure took place in the interlobular area where arteriovenous anastomoses existed.

Herrick (1907) further found that on perfusing cirrhotic livers there was no obstruction to the portal blood flow. However, it was found that the portal pressure in cirrhosis was markedly influenced by the pressure at which fluid

passed into the liver through the hepatic artery—1 mm. rise in portal pressure for every 6 mm. of arterial pressure—whereas the effect of arterial rise in pressure did not effect the portal pressure in normal livers until it had passed the 100 mm. mark, and in cirrhotic livers the effect on the portal pressure was evident at 30 mm. of arterial pressure.

On the other hand, McIndoe's studies (1928) on cirrhotic livers "in situ," were in seeming conflict with Herrick's findings. McIndoe found that whereas in a normally perfused portal vein 100 per cent of the perfusion fluid could be recovered from the hepatin vein, only 13 per cent could be recovered in the cirrhotic liver. A much greater quantity of fluid was obtained from the hepatic vein on perfusion of the hepatic artery of cirrhotic livers. As the cirrhosis increases, the portal blood no longer supplies the liver, which is fed by the hepatic artery. The interlobar fibrosis may increase to the point of obliterating the arterial flow also. It is at this point that liver insufficiency or hemorrhage may be explained by the particular rate of obliteration of blood flow to the liver.

Vascular Bed of the Spleen.—The importance of the intrasplenic circulation in portal hypertension necessitates a brief review of the vascular anatomy of the spleen (Maximow and Bloom, 1943). The branches of the splenic artery enter the hilum and pass along the trabeculae, with which they branch repeatedly, becoming progressively smaller in caliber. They are muscular arteries of medium caliber and have a loose tunica adventitia surrounded by the dense connective tissue of the trabeculae. The artery leaves the trabeculae and enters the white pulp of the spleen. There it is covered by a sheath of lymphoid tissue (white pulp). Throughout its course within the white pulp, the artery gives off numerous capillaries which supply the lymphatic tissue of the sheath. These arterial capillaries pass into the red pulp to unite with venous sinuses. Before uniting, each branch is provided with a characteristic spindle-shaped thickening of its wall, the Schweigger-Seidel sheath. Further branching takes place, and then the union with the veins is accomplished. It is this union with the veins that is subject to much dispute.

There are three main theories as to how blood gets from the arteries to the venous sinuses (Maximow and Bloom): (1) The arterial capillaries open directly into the spaces between the reticular cells of the splenic cords and the blood gradually filters into the venous sinuses. This is known as the "open" circulation theory. (2) The arterial capillaries communicate directly with the lumen of the venous sinuses, this being the "closed" circulation theory. (3) The compromise theory that holds that both types of circulation exist at the same time.

Weidenreich (1901) ingeniously tagged some corpuscles and studied their fate in the spleen of a rabbit. Tagging was accomplished by using the blood of birds, which is nucleated. After injecting, he waited for several minutes and then sacrificed the animal and prepared sections of the spleen. He found the nucleated erythrocytes of the bird in the pulp spaces and concluded that the capillaries of the spleen open out into the splenic pulp.

Helly (1903), on the other hand, repeating the experiments came to another conclusion. He believed that the bird erythrocytes passed from the arterial

capillaries into the venous sinuses and from there through the clefts in the sinus wall into the pulp.

MacNeal and Patterson (1926) attempted to see which of the two was right. They repeated the experiments and killed the animals in one minute. If Weidenreich was right, the nucleated erythrocytes would be numerous in the pulp, whereas if Helly was right they would be numerous in the sinuses. Weidenreich proved to be right.

Robinson (1928) reviewed Mall's studies (1902) and his own and concluded that the circulation of the spleen is by the open method. The control of circulation through the spleen is by contraction of the fibromuscular element in the trabeculae.

MacNeal, Otani, and Patterson (1927) suggested that the circulation in the spleen is essentially an open circulation. The pulp spaces constitute the connecting channels through which the blood passes from the arterial capillary to the venous sinus. This mechanism brings about intimate contact of the blood plasma with the cellular elements of the follicle, and a similar intimate contact between the formed elements in the blood and the reticuloendothelial elements of the marginal zone and the pulp cord.

Knisely (1936) in his study of living mice, rats, and cats suggested that "open" or "closed" system nomenclature be dropped. His studies showed that the system in the spleen consists of pre-formed, interconnected, lined channels. The venous sinuses quantitatively separate the cells of the blood from the fluid in two ways: (1) filtering-filling process followed by a storage phase and (2) continuous filtration process. The sinus wall, he claimed, is capable of considerable variability. During digestion, the storage phase is increased and the spleen is large. During the filtration-filling phase the venous sinus linings are freely permeable to the colloids of the blood. During the conducting phase, fluid does not pass out through the sinus wall.

The venous sinuses store the cells for various periods of time. Under some circumstances incoming blood cells are stored and previously stored cells are released synchronously, so that the total volume of stored cells may be increased or decreased. Whole blood can pass through the spleen, without having its cells separated from its fluid, by two different routes: (1) by sinuses and sinus systems which are in the conducting phase and (2) capillaries conducting blood which nourishes the tissues during the long storage phases of the sinuses.

Control of inflow and outflow of blood is by the sheaths of Schweigger-Seidel. The venous sinuses, Knisely claimed constitute a mechanism which acts upon blood.

More recent studies by MacKenzie, Whipple, and Wintersteiner (1941) using the general technique of Knisely (1936) suggested that with improvements in technique one may come to the opposite conclusion, that is, the circulation in the spleen is open.

The Sphincter Mechanism of the Cardia.—The problem of the presence or absence of a true anatomic cardiac sphincter has continued for a long period of time. Meltzer (1883) found by stethoscopic methods that swallowed foods did not squirt directly into the stomach but were checked a short distance above the

cardia. A succeeding peristaltic wave, about six or seven seconds later, pressed it onward into the stomach.

Fleiner (1900), Zaaijer (1923), and Jackson (1927) have denied the existence of a sphincter at the cardia. Hurst (1925), Abel (1929), and Mosher (1930) are proponents of the sphincter theory.

Lendrum (1937) demanded three morphologic details as proof of the anatomic existence of a sphincter: (1) a distinct band of circular muscle marked off from the adjoining muscle by connective tissue septa; (2) an associated dilator muscle formed by the dipping into the circular muscle of longitudinal fibers and (3) a local thickening of circular muscle which persists after the factor of local spasm has been eliminated. He concluded after careful study of 150 human cardias, that a sphincter is not present morphologically.

Whether or not a sphincter is present is not within my scope to decide. However, cardioesophageal relaxation with regurgitation of barium can be shown by x-ray view (Robins and Jankelson, 1926).

Therefore it may be suggested from the evidence at hand, that although it does not occur in all cases, regurgitation of gastric contents may occur frequently enough so that it may be an etiological factor in esophageal pathology.

Pathogenesis of Portal Bed Obstruction

Patients with portal hypertension were divided by Whipple (1945) into two main groups. Group I includes those having intrahepatic portal block, and Group II those having extrahepatic portal block. The first group includes the cirrhoses, while the second includes cases of fibrous replacement and/or thrombosis of the portal vein or of a main tributary, and cavernomatous transformation of the portal vein or its tributaries.

I believe it to be beyond the scope of this paper to discuss extensively the cirrhoses of the liver. Suffice it to say that portal hypertension does exist associated with splenomegaly in cirrhoses of the liver (Frerichs, 1879, Snell, 1931, Brandberg, 1935, Henrikson, 1936, Eppinger, 1937).

Splenic Anemia or Banti's Syndrome.—When Banti described the disease entity which bears his name, little did he know of the controversy that would rage as a result. After working since 1882, he finally published his observations in 1894. Osler first drew attention to the clinical aspects of this disease.

The *etiology* of the syndrome is varied. Infection has been indicted by some. Gibson (1919) has isolated a streptothrix, Yates (1919) a diphtheroid bacillus, and Hollins (1919) the colon bacillus. Leon-Kindberg (1914) felt that the lesions resembled those of a plasmodian infestation. Gregoire, Weil, and Flandrin (1927) reported a case in which the spleen was loaded with mycelial threads and spores. Banti (1894) suggested a toxin as a cause.

It is entirely probable that the entire picture of Banti's syndrome may be caused by various mechanical disturbances of the portal system. It is easy to see how the confusion of separating this syndrome from pure cirrhosis arises. There is a great deal of overlap. However, as will be shown, there are authors who believe Banti's syndrome may occur without cirrhosis.

The mechanical factors that have been proposed in Banti's syndrome are as follows:

1. *Thromboses of the splenic and/or portal veins.* (Warthin, 1910, Opitz, 1924, Rosenthal, 1925, Wallgren, 1927, Wilson and Lederer, 1929, Noble and Wagner, 1933, Mallory, 1934, Smith and Farber, 1935, Klemperer, 1938.)
   (a) Various inflammations of the upper abdomen (pancreatitis, etc.).
   (b) Acute infectious diseases.
   (c) Infectious processes in spleen itself.
   (d) Primary degeneration in vein wall akin to atherosclerosis of arteries.
   (e) trauma.
2. *Cavernomatous transformation of the portal vein.* Beitzke (1910) and Hart (1913) were of the opinion that this is a typical congenital malformation. Risel (1909), Verse (1910), and Emmerich (1912) believed that the cause of this must be sought in a thrombosis of the portal vein followed by organization and recanalization. Pick (1909) on the other hand argued that this is a neoplastic lesion, an angioma, or cavernoma of the hepatoduodenal ligament, inasmuch as in some cases the process extends far beyond the limits of the portal vein.
3. *Stenoses of the portal vein* (Leon-Kindberg, 1914):
4. *Compression of the portal or splenic veins from without:*
   (a) Adhesions from previous peritonitis (Smith and Farber, 1935)
   (b) Enlarged lymph nodes (Smith and Farber, 1935)
   (c) Gallstones (Armstrong, 1906)
5. *Congenital narrowing of the portal bed in liver* (Moschkowitz, 1917).
6. *Cirrhosis of the liver.*
7. *Congestive splenomegaly without cirrhoses* (Rolleston, 1914, Larrabee, 1934, Eppinger, 1937, Rousselot, 1940).

When Banti (1894) described the disease entity which bears his name, he mentioned three phases: (1) anemic phase with splenomegaly, asthenia, and occasional gastrointestinal hemorrhages; (2) transitional stage with oliguria, urobilinuria, hepatomegaly, pigment disturbances of the skin and increasing gastrointestinal disturbances; (3) ascitic stage with atrophy of the liver, hemorrhage, and death.

The pathologic pathognomonic lesion he described as a conspicuous thickening of the fibrillar reticulum around the central arteries of the malpighian corpuscles. These were known as fibroadenia.

Klemperer (1938) found definite fibroadenia of the malpighian corpuscles in thrombophlebitic splenomegaly and in cases of obliteration of the splenic and portal veins, in hepatic cirrhoses, and in Cooley's anemia.

To quote Klemperer, "The clinical picture is not characteristic and the histologic splenic lesions are not specific. A diagnosis in the early anemic period cannot be made with any degree of certainty. The alleged favorable results of splenectomy of this stage cannot be used as a basis for diagnosis of this disease

because there is no evidence to prove that the progress of the disease was actually arrested. An improvement in the late cirrhotic stage also does not help to identify such cases because similar successful results after splenectomy have been reported in undoubted 'primary' liver cirrhoses. From the foregoing considerations it becomes apparent that the clinical symptoms likewise do not justify the recognition of Banti's disease as a distinct morbid entity."

Johnston (1931) suggested that age and location of pathology are related. Younger individuals respond with splenomegaly long before older individuals do.

Collateral Circulation of Portal Obstruction.—In order for blood to be conveyed to the heart in cases of obstruction of the portal vein, communications exist between the portal vein and vena cava which may become enlarged.

Kegaries (1934) stated, "It is probable that the capillary-like anastomosis at the cardia offers a marked resistance to the flow of blood from the portal to the systemic veins as in the case when the portal circulation becomes obstructed. In such instances the increase of venous pressure must exert itself upon the veins below the cardia for some time before the resistance of the cardia is overcome. Varices result from an increased flow of blood through a vein and an inability of the muscular and elastic fibers to withstand an increased intravenous pressure at the cardia; and as has been noticed previously the submucous veins of the esophagus are well supported and it is reasonable to believe that the formation of varices first occurs below the cardia and secondly above that point after collateral channels of the anastomosis have been established. Where several veins of large caliber cross the cardia, the formation of varices above the cardia is probably more rapid. When present they are no doubt the first veins in the region of the cardia to become enlarged."

The collateral channels developed between the portal and caval systems in intrahepatic block were classified by McIndoe (1928) as follows:

> 1. At the two situations in the gastrointestinal tract where absorbing epithelium comes in contact with protective epithelium, that is, at the cardia and anus. The veins at the cardia anastomose with the azygos and diaphragmatic veins of the caval circulation. The veins at the anus furnish an outlet to the inferior vena cava by way of the hemorrhoidal veins.
>
> 2. At the site of an obliterated embryologic circulation, such as the falciform ligament containing the para-umbilical veins.
>
> 3. At all situations within the abdomen where the gastrointestinal tract, its appendages, or the glands developed from it become retroperitoneal developmentally or adherent to abdominal walls pathologically. This includes the duodenum, small intestine, colon, omentum, spleen, and pancreas, containing the veins of Retzius, and the liver with its accessory veins of Sappey.

It must be recalled that Rousselot (1940) has pointed out that congestive splenomegaly may or may not be accompanied by a hypertension of the left gastric vein of the stomach depending upon the anatomic configuration of the emptying of this vessel. If the vein empties into the portal vein directly, a

thrombosis of the splenic would not be expected to cause any increase in pressure in the coronary vein. If, however, emptying takes place into the splenic vein and thrombosis occurs distal to this, then the reverse would occur.

Snell (1931) described the presence of rather unusual types of collateral development in the axilla and about the umbilicus. Eppinger (1937) studied the incidence of dilatation of subcutaneous veins in the region of the abdomen and found these to be developed in 22 per cent of cases in portal cirrhosis.

It is more important to speak of the incidence of hemorrhage associated with portal hypertension than of esophageal varices, as these are difficult at times to demonstrate. The incidence varies from 10 to 40 per cent (Preble, 1900, Rolleston, 1914, Eppinger, 1937).

Experimental Production of Portal Bed Block.—Various methods have been used to produce portal hypertension. Occlusion of the splenic veins of dogs and rabbits as it came off the spleen by Warthin (1910) resulted in temporary distention of the spleen, with eventual fibrosis. Simonds (1936) has attempted to produce experimental cirrhoses by obstructing the hepatic veins for varying periods of time. However, degenerative changes were observed after this procedure which did not resemble cirrhosis. More recently Brunschwig and his associates (1945) have been able to occlude the portal vein gradually. Kershner, Hooton, and Shearer (1946) have been able to produce portal hypertension by occlusion of the inferior vena cava above and below the liver. Rousselot and Thompson (1939) have produced cirrhosis in dogs by injecting silica repeatedly into the splenic vein. After two years a very large spleen develops with very extensive collateral circulation and esophageal varices.

Moon (1934), in an extensive review of the subject, enumerated the agents that have been used with more or less success in the production of cirrhoses. These were grouped as inorganic chemicals, organic substances, serologic agents, and infections. In many instances combinations or agents were found more effective than any of the agents alone.

Inorganic agents: Phosphorus, arsenic, lead, potassium salts, thorium dioxide, manganese, copper.

Organic substances: Alcohol, chloroform, tar, carbon tetrachloride, cholesterol, butyric acid, aleuronat, tobacco, ammonium carbonate, putrid horseflesh, phenol hydrazine, hydrochloride cinchophen, antipyrine.

Serologic agents: Antihepatic serum, immune serums, hepatolytic serum.

Infectious agents: Various bacteria injected intravenously.

More recently Nelson, Fitzhugh, and Calvery (1943) have caused cirrhoses of rats with selenium. Various dietary deficiencies have also come in for their share in cirrhoses production.

It must be said that it is probable that the majority of these substances may have no connection with the development of human cirrhoses, but serve to complete a better understanding of the disease.

Liver Regeneration.—Since Volerian (1894) first noted the ability of the liver to regenerate, Mann and his co-workers (1931) have studied this interesting

aspect of liver pathology. Higgins and Anderson (1931) studied the regeneration of rat's liver after hepatectomy and found a cyclic activity during the restorative period. The most rapid restoration occurred during the third day. In the period of four to seven days the liver was less active cytologically, except for a marked increase in the intake of fluid.

Mann, Fishback, Gay, and Green (1931) tested the effect of diverting the portal blood on the restoration of the liver after partial hepatectomy. Whereas partial removal of the normal liver is always followed by restoration of hepatic tissue, such regeneration did not occur when the portal blood was diverted.

In testing the effect of cirrhosis on liver regeneration, these same authors noted that when 30 per cent or more of the cirrhotic liver was resected and only a moderate degree of cirrhosis was present, some restoration occurred in the remaining portion. But when the liver was completely cirrhotic no regeneration occurred.

Higgins, Mann, and Priestley (1932) determined the effect of increased blood delivered to the liver on its regeneration. Anatomically the venous drainage of the chicken suited their purposes very adequately. These experiments showed that when blood was diverted into the portal vein after hepatectomy, the regrowth of the liver was even greater than normal.

The role of the portal circulation in normal liver regeneration was emphasized by Mann (1940). However, its exact role in regeneration of injured liver is not known. He postulated that, in all probability, regeneration takes place in areas of the liver that are not injured. Concomitantly the toxic agent is still working and destruction is taking place at another area. Eventually the liver is replaced and the portal circulation and regeneration impeded.

Blood Flow Determinations in the Liver.—In various studies of portal hypertension it is important to know various blood flow and pressure measurements of the liver portal flow. Stromuhr measurements have been used as well as gaseous metabolism readings.

Lichtman (1942) reported the proportions between portal and hepatic inflow as reported by various authors as shown in Table I.

TABLE I

	PERCENTAGE THAT HEPATIC ARTERY CONTRIBUTES TO TOTAL INFLOW
Burton-Opitz (1911)	24-44
Barcroft and Shore (1912)	34
MacLeod and Pearce (1914)	26-32
Bauer, Dale, Paulsson, and Richards (1932)	25-30
Schweigk (1932)	20-25
Blalock and Mason (1936)	12.6-24.5
Grindlay, Herrick, and Mann (1941)	12-22
Snyder (1942)	14

Studies on the amount of blood coming from the abdominal organs to form the portal venous flow have been made by Burton-Opitz:[26-30]

Total portal inflow to the liver, 4.92 c.c. per sec.
Intestinal flow to the liver, 2.74 c.c. per sec.
Gastric flow to the liver, 1.23 c.c. per sec.
Splenic flow to the liver, 0.95 c.c. per sec.

Thus, both the stomach and spleen combined produce about 44 per cent of the total portal inflow.

Various observers have measured the normal portal pressure in human beings. Bellis (1942) found that it varied from 14 to 22 cm. of water. Roussellot (1939) found that it varied between 7 and 22 cm. of water.

The portal vein differs from other veins in that it divides into numerous branches which ultimately form a rich capillary network within the liver substance. In this it resembles an artery, but unlike an artery it is interposed between two capillary beds, one in the liver and the other in the splanchnic area which it drains. In order that the portal blood be filtered through the capillaries of the liver and then on into the systemic veins, the pressure in the portal vein must normally be higher than that of the systemic veins. Blakemore and Lord (1945) have measured the portal pressures in their cases of hypertension and have found them to be from 260 mm. of water to over 500 mm. of water. Blakemore and Lord (1945) took pressure readings in all the branches of the portal before determining their therapy.

Importance of Acid and Vascular Factors in the Ulcer Diatheses

It is not within the scope of this paper to review the literature on the pathogenesis of ulcer. Recent work by Hay (1942), Code and Varco (1940), Merendino (1945), Lannin (1945), Kolouch (1945), and Baronofsky (1945, 1946), working in Wangensteen's laboratory (1945) at some time, has shown that the acid factor and the vascular factor are important in ulcer diatheses. An excellent review by Lannin (1945) included a good deal of the historical and experimental evidence of the acid factor in ulcer.

Therapy of Bleeding Associated With Portal Hypertension

There have been various methods, surgical and medical, attempted in the treatment of hematemesis associated with portal hypertension. (See Table II.) In cases of cirrhosis, wherein the functioning liver tissue has been diminished to the point of no longer producing prothrombin, the simple prothrombin test of Quick (1942) will demonstrate this deficiency. The bleeding due to lack of this factor, so essential in blood clotting, can be quickly corrected by addition of Vitamin K therapy and transfusion.

Crafoord and Frenckner (1939) first proposed injection of esophageal varices through an esophagoscope. Moersch (1940) in this country has been the keenest exponent to this type of therapy.

Drenckhan (1939) presented an interesting physiologic approach in the treatment of esophageal varix bleeding. He claimed that the primary difficulty in this type of bleeding is increased resistance to blood flow through the liver. According to Poiseuille's law, three factors exist in causation of back pressures: (1) the length and radius of the vessel, (2) blood volume, and (3) viscosity of blood. The factor of viscosity can be altered by venesection, since it had been shown that the higher the cell count, the more viscid the blood. Viscosity of blood increases slowly until the corpuscle concentration of 50 per cent is reached. From this point, viscosity climbs rapidly. A case is presented in which venesection was used successfully as treatment for hematemesis in Banti's disease

TABLE II. HISTORICAL SUMMARY OF SURGICAL TREATMENT OF PORTAL HYPERTENSION

AUTHOR REPORTING	DATE	OPERATION
1. Banti	1894	Suggested splenectomy which was reported in a later publication
2. Drummond and Morison	1896	Omentopexy for ascites
3. Talma	1898	Reported original cases of Von Maulen (1889) and Schelky (1891); omentopexy
4. Rafferty	1900	Unsuccessful case of splenectomy
5. Vidal	1903	Eck Fistula: Portal vein implanted into vena cava; successful, lived 4 months
6. Ruotte	1907	Implantation of saphenous vein into peritoneal cavity for ascites
7. DeMartel	1910	Side-to-side anastomoses of vena cava and portal vein; died of anuria
8. Handley	1910	Internal drainage of ascites into thigh area by means of silk threads
9. Paterson	1910	Glass button procedure draining ascites into subcutaneous tissues
10. Villard and Tavernier	1910	Anastomosis of ovarian vein to superior mesenteric vein
11. Gunn	1911	Anastomosis of right ovarian vein and portal vein
12. Lanz	1911	Transplantation of the testicle and spermatic cord into the peritoneal cavity and surrounding them with omentum
13. Lenoir	1912	Eck fistula; anastomosis of portal vein to inferior vena cava
14. Rosenstein	1912	Drainage of ascitic fluid directly into bladder
15. Meursing	1912	Anastomosis of spermatic vein to splenic vein
16. Bogoras	1913	Transplantation of superior mesenteric vein into the inferior vena cava
17. Mayo, W. J.	1919	Splenectomy; report on cases at Mayo Clinic since 1905
18 Flerow	1926	Ligation of left gastric artery, the right and left gastroepiploic arteries, and the inferior mesenteric veins
19. Walters, Rowntree, and McIndoe	1929	Ligation of left gastric veins
20. Westphal	1930	Compression with balloon of bleeding esophageal varices
21. Holman	1933	Ligation of splenic artery followed by implantation of spleen into abdominal wall
22. Drenckhahn	1939	Venesection if hemoglobin above 50 per cent
23. Crafoord and Frenckner	1939	Injection by means of esophagoscope of sclerosing solution into varicosed esophageal veins
24. Whipple, Blakemore, and Lord	1945	Nonsuture anastomosis of portal vein to inferior vena cava and splenic to renal veins
25. Baronofsky and Wangensteen	1945	Demonstration of abetment of ulcer diatheses (histamine-provoked) by portal hypertension
26. Wangensteen	1945	Performance of extensive gastric resection (95 to 98 per cent) for hematemesis of portal hypertension
27. Blalock, Blakemore	1946-1947	Anastomoses of splenic and renal veins, end-to-side
28. Phemister and Humphreys	1947	Total gastrectomy and gastroesophageal resection

when splenectomy failed to relieve. Walters, Rowntree, and McIndoe (1929) have ligated the left gastric vein and its tributaries in an attempt to prevent blood flow to the obstructed portal vein. Talma (1898) suggested increasing the vascular connections between the systemic and portal systems by forming adhesions: (a) between the omentum and the anterior abdominal wall, (b) between the liver and the spleen with the vault of the diaphragm on the anterior abdominal wall, and (c) between the gall bladder and the anterior abdominal

wall. Bogoras (1913) implanted the superior mesenteric vein into the superior vena cava in an attempt to by-pass the cirrhotic liver and therefore decrease the hypertension.

Flerow (1926) suggested the ligation of the left gastric artery, the right and left gastroepiploic arteries, and the inferior mesenteric vein. By ligation of the several arteries carrying the blood supply to the stomach, the veins of the stomach will receive their blood supply mainly from the portal vein by a reverse flow of blood from this vein. However, as will be shown later, an increase of blood flow through the stomach will add to the bleeding ulcer-erosion diathesis.

Whipple (1945) recently performed successfully the Eck fistula technique of diversion of the portal blood into the caval flow, thus attempting a reduction in pressure. This procedure had been tried in earlier years by various men with unsuccessful results. Blakemore (1946) reported several patients with recurrent episodes of bleeding in a follow-up study of the group subjected to surgery at Columbia. Fourteen patients were operated upon. Four had extrahepatic obstruction, while in the ten remaining the site of the portal obstruction was intrahepatic due to the portal cirrhosis. There were two operative deaths. Three of the four patients with extrahepatic block had episodes of bleeding after operation, but the bleeding episodes were not as severe or as frequent as before operation.

Splenorenal anastomosis after excision of both the spleen and kidney was performed in one-half of the cases followed postoperatively. All but one of the remainder of the patients had an anastomosis of the portal vein to the vena cava, and the exception had an anastomosis of the splenic vein to the vena cava.

The method and location of the anastomosis have received some consideration. In his earlier report, Blakemore (1946) used the nonsuture end-to-end anastomosis in the splenorenal type. More recently an end (splenic)-to-side (renal) with preservation of the kidney was used (Blakemore, 1947). No mention was made, however, concerning the nonsuture technique. On the other hand, Blalock (1947) preferred the use of suture technique in the end-to-side splenorenal vein anastomosis.

The therapy of bleeding associated with portal hypertension has not been too successful. The procedures other than Whipple's have been repeatedly tried, with a follow-up that hardly warrants any further trial. The most important element, that seems to be forgotten, is the fate of the so-called "esophageal varices" even after treatment.

The reports upon the results of the Eck fistula procedure are yet too early to permit critical evaluation; moreover, that bleeding is not completely eliminated is evident in Blakemore's (1946) report.

Comment and Reaffirmation of the Problem

The problem of hematemesis associated with the hepatosplenopathies has long been a vexing one. The association of portal-bed block and the resultant portal vein hypertension has been accepted as one of the main etiologic agents necessary before hemorrhage into the upper intestinal tract can occur. However, the nature of the bleeding of so-called "esophageal varices" is a little mystifying.

Why cannot blood backed up into the portal veins flow easily into the systemic veins? There is no real gravity problem as in varicose veins of the lower extremity and hemorrhoids. Patients with obstruction of the superior vena cava exhibiting esophageal varices apparently do not bleed. Kaufmann (1929) noted that varices are rare in the upper part of the esophagus, and are only seen in advanced age or in cases of congestion of the superior vena cava as in malignant goiter.

It hardly seems reasonable to assume that mere hydrostatic distention of these veins and the eventual rupture is the sole cause of the hematemesis. More recently Baronofsky and Wangensteen (1945) have shown that, with impairment of the nutrition of the mucous membrane of the stomach, duodenum, and esophagus, due to venous pooling, these areas are lowered in resistance and will be easy prey to the gastric digestive juices.

Franklin (1937) stated that the pressures required to rupture healthy veins are such that they are incompatible with an efficient circulation. In the healthy body rupture of a vein by increase of internal pressure is extremely rare. For one thing the veins are on the whole more resistant than the capillaries drained by them. Grehant and Turnquand (1885) came to the conclusion that the veins of an animal normally require a slightly higher internal pressure for their rupture than do the carotid arteries of the same animal. Kegaries (1934) has shown that the veins of the lower end of the esophagus are well supported with connective tissue. Perusal of the literature suggests that in bleeding of esophageal varices, the way to demonstrate these is to inject them. However, sometimes even this procedure fails. Is one then to assume that this is a failure in technique? Preble (1900) in a review of sixty cases of gastrointestinal bleeding due to cirrhosis puts forth protocols. Quite a few of the cases present ulcers or erosions of the mucous membrane of the stomach. Debove and Courtois-Suffet (1890) presented fourteen cases in which there were no demonstrable lesions of the mucous membranes, but many erosions of the cardia were present.

Various observers at one time or other claim the beneficial effect of splenectomy may be attributed to removal of about 40 per cent of the total circulating portal blood volume. That statement in itself would be open to question. If this one organ, the spleen, supplies 40 per cent of the portal blood volume, then the entire small intestine, large intestine, pancreas, and stomach supply only 60 per cent of that blood volume. That this is not so was shown by Burton-Opitz (1911). He found that the stomach and spleen together supply about 44 per cent of the blood, the spleen itself less than 18 per cent. On the other hand, one must remember that these studies were made on normal animals. Perhaps with portal hypertension and a very much enlarged spleen, the organ percentage of portal blood flow changes.

Regurgitation of gastric digestive juice into the esophagus is not an uncommon occurrence. There is evidence presented that there may not be present in the normal human cardia a true morphologic contractile muscle, instead only a physiologic sphincter. Friedenwald, Feldman, and Zinn (1928) showed that acid has a deleterious influence on a diseased or injured esophageal mucosa.

Why then cannot the mucosa that is poorly nourished, due to stasis of portal hypertension, be subject to the eroding effect of gastric contents?

Recently Whipple (1945) has utilized the ingenious nonsuture anastomosis of Blakemore and his associates in creating an anastomosis between the portal vein and the inferior vena cava. There is an attempt therefore at the reduction of the high portal pressure by a short circuiting procedure (Eck fistula). A recent follow-up study of fourteen patients so treated has shown that some of the patients have had episodes of bleeding since operation and post-mortems on some have shown occlusion of the anastomosis. Some vascular surgeons may attribute this to the method of anastomosis. They claim an end-to-end direct suture anastomosis might be better. Blalock (1945) in a communication to Whipple stated that two of his patients have died since operation from recurrent bleeding from esophageal varices. More recently Kelsey, Robertson, and Griffin (1947) have offered pathologic evidence that may explain the failure of such anastomoses to work. They found that in many cases of diseases associated with portal hypertension, a chronic inflammatory process was present in the majority of its branches. That the Eck fistula procedure fails in some cases is evidenced by recurrent bleeding episodes.

Reconsideration of the Problem

With the evidence at hand, at the suggestion of Dr. Owen H. Wangensteen, it seemed best to explore the factor of gastric resection for portal hypertension. This procedure in portal hypertension would work on three theses:

1. If the acid peptic factor of gastric secretion is important in the causation of erosions in the esophagus, then extensive or total gastrectomy would eliminate this.

2. If the stomach drains into the portal circulation and the esophagus into the caval, and there is a communication between the two, then isolation of the esophagus from the portal circulation by means of gastrectomy should prove satisfactory in preventing hemorrhage.

3. If extensive gastrectomy were done, there would be an additional reduction of blood inflow into the portal system over that attending splenectomy.

It is, therefore, our purpose to explore these theses experimentally and to present clinical cases in which this procedure has been tried.

DESCRIPTION OF THE EXPERIMENTAL METHODS, OPERATIVE PROCEDURES, RESULTS, AND CLINICAL CASES

Ligature of Splenic Vein and Cellophane Around Portal Vein.—In a previous publication (Baronofsky and Wangensteen, 1945), we have described methods by which portal hypertension may be simulated within the stomach. In the series of experiments described, a partial obstruction to the normal venous return of blood from the stomach to the portal system was made. Two methods of obstructions were used. In one, the lesser omental bursa was entered by retracting the stomach upward and to the left; an avascular area in the omentum was opened as it came off the greater curvature of the stomach. The splenic vein was identified and dissected down to its junction with the left gastric vein.

Ligatures were then placed proximal to this junction and distal to where the inferior mesenteric vein entered the splenic vein (Figs. 1 and 2). The splenic vein was then cut between these ligatures. The left gastroepiploic vessels were then divided and ligated about at the mid-point of the greater curvature. An additional ligature and division was made of the right gastric vein at the antrum.

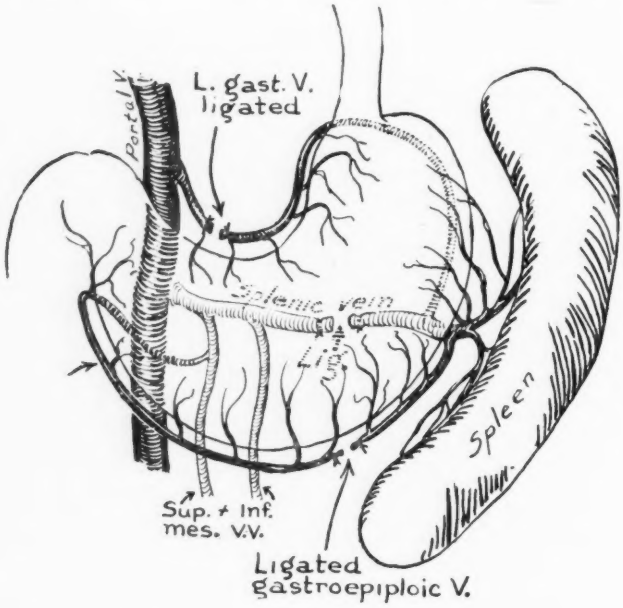

Fig. 1.—Sites of ligature of splenic and left gastric veins, as employed in these experiments.

Fig. 2.—The anatomy of the venous drainage around the stomach of a dog is shown. The junction of the left gastric vein and the splenic vein is shown immediately above the middle finger of the lower hand. It is at this point that the ligature is placed.

Pearse (1940) has shown that cellophane, when placed around the aorta, will slowly obliterate this vessel, an occurrence occasioned through the agency of a severe fibroblastic reaction within six weeks of the placement of the cellophane ligature. This led us to make use of cellophane as a constricting agent in one of the series of experiments. The same approach was used. Upon identifying the portal vein as it lay in the gastrohepatic omentum, it was dissected for a distance of 1 cm. or more. A piece of cellophane was placed snugly around it.

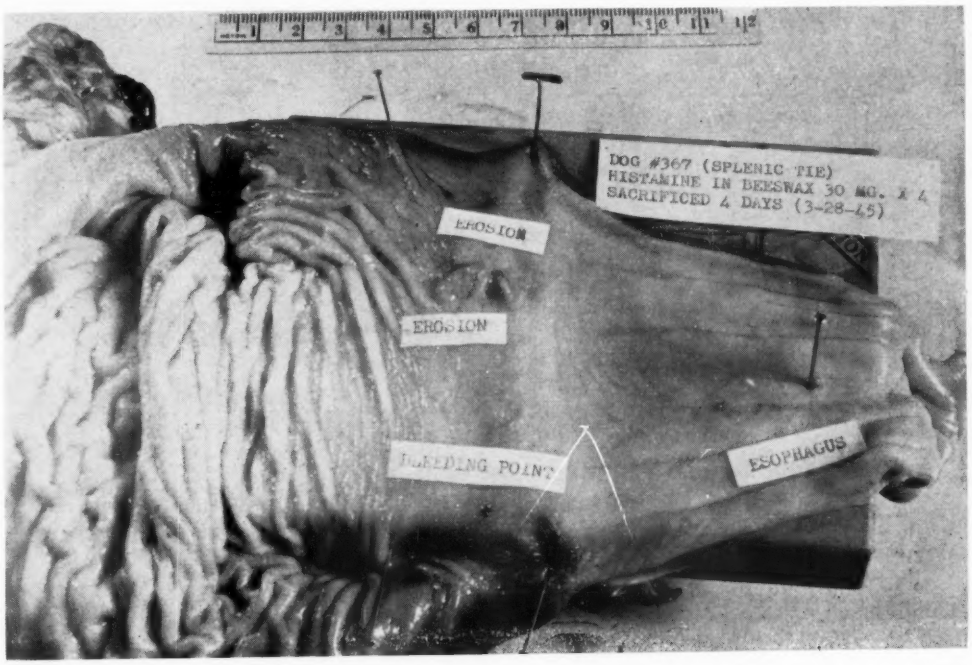

Fig. 3.—Erosions and bleeding points in a dog with ligature of the splenic vein, histamine-in-beeswax had been given four days.

Fig. 4.—Perforated duodenal ulcer and multiple gastric ulcers in the stomach of a dog after only three injections of histamine-in-beeswax (30 mg.). A complete obstruction of the portal vein had been obtained by placement of a cellophane tie 150 days previously.

This was knotted, care being observed that this procedure did not cause an immediate complete obstruction of the portal vein.

The animals were then subjected to histamine-in-beeswax. The results obtained made it apparent that obstruction of the venous drainage from the stomach abets the ulcer diathesis. That is, erosions and ulcer are far more readily provoked with histamine in the presence of portal hypertension than when there is no obstruction to venous outflow of blood from the stomach (Figs. 3 and 4). Hay, Varco, Code and Wangensteen (1942) have shown the difficulty of producing ulcer in rabbits, by histamine alone. In the dog and rabbit ulcers were produced regularly in a surprisingly short time when the venous drainage of the stomach was obstructed, accompanied by the simultaneous administration of histamine. Esophageal varices were observed regularly in the experiments of longer duration in which the portal vein was obstructed.

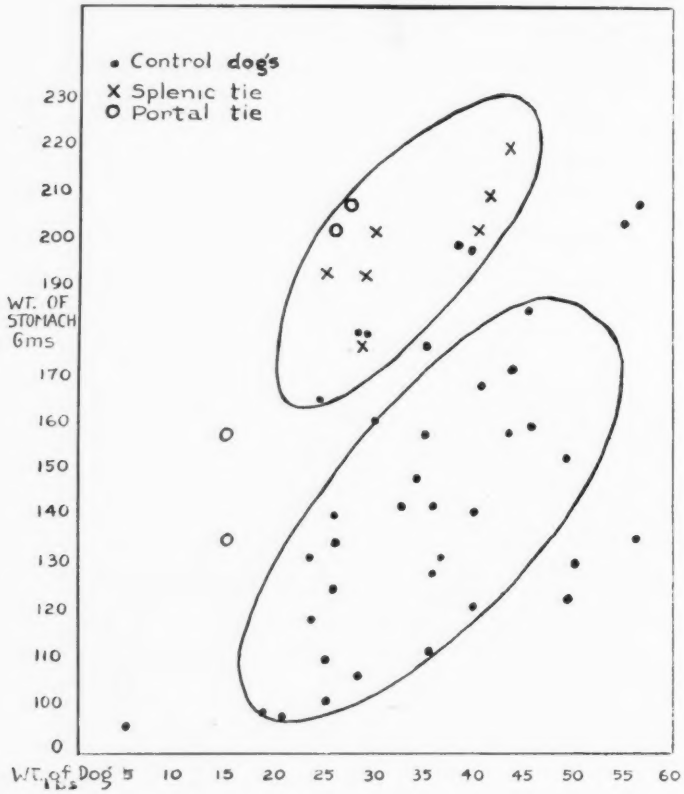

Fig. 5.—Scatter graph showing heavier weights of the stomachs of dogs with splenic vein ties and portal vein obstruction. Thirty-seven control dogs, four dogs, with cellophane about the portal vein, and seven dogs with splenic vein tied were used.

Another striking finding was the uniform increase in weights of the stomach of both rabbits and dogs in which obstruction to the venous outflow from the stomach had been established (Fig. 5). Microscopically this occurrence appeared to be due to an enema of the entire gastric wall, but especially of the mucosa and submucosa (Fig. 6).

Extensive Gastric Resection for Bleeding Associated With Portal Hypertension.—To test the validity of the hypothesis that the bleeding from gastric and esophageal erosions, which can be created experimentally by the administration of histamine in the presence of portal obstruction, can be prevented by

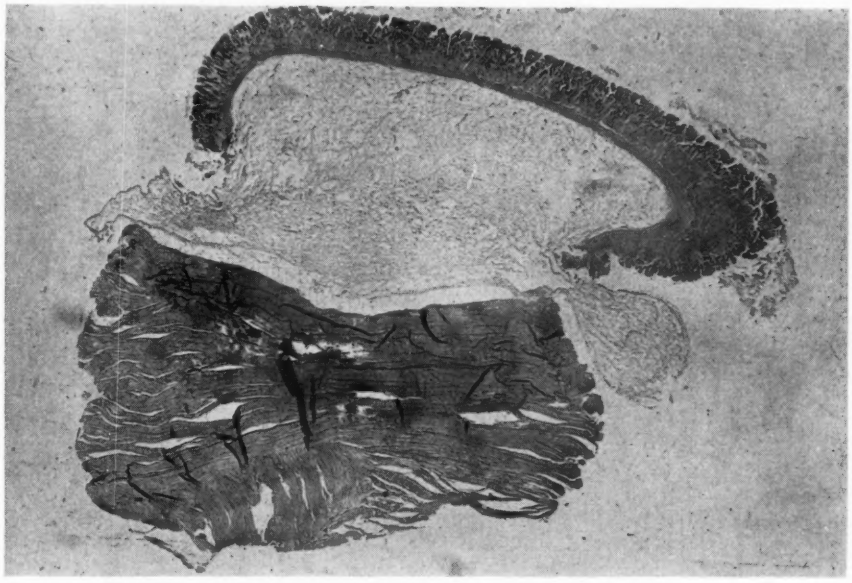

Fig. 6.—Marked edema of submucosa of stomach in a dog after ligature of left gastroepiploic, and junction of left gastric and splenic veins.

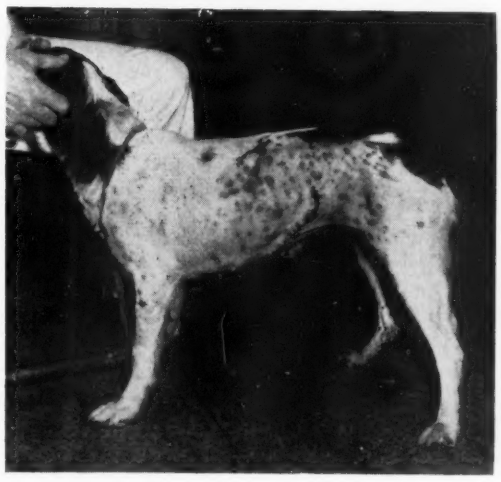

Fig. 7.—A dog in which an extensive gastric resection had been done by means of a side incision. The incision is subcostal and is made with the dog lying on his side.

preliminary extensive gastric resection, the following experiments were carried out on dogs in two series. In one series a standard three-quarter gastric resection with short afferent loop was performed. In the other series, an extensive gastric resection (90 per cent) was made, with a short afferent loop. In both series the aseptic clamp technique was used.

The anesthesia used was the same as in the splenic tie series. When extensive gastric resection was performed, it was found most convenient to put the animal on his side and use an extended subcostal incision. Exposure thus obtained was more than adequate (Figs. 7, 8, and 9).

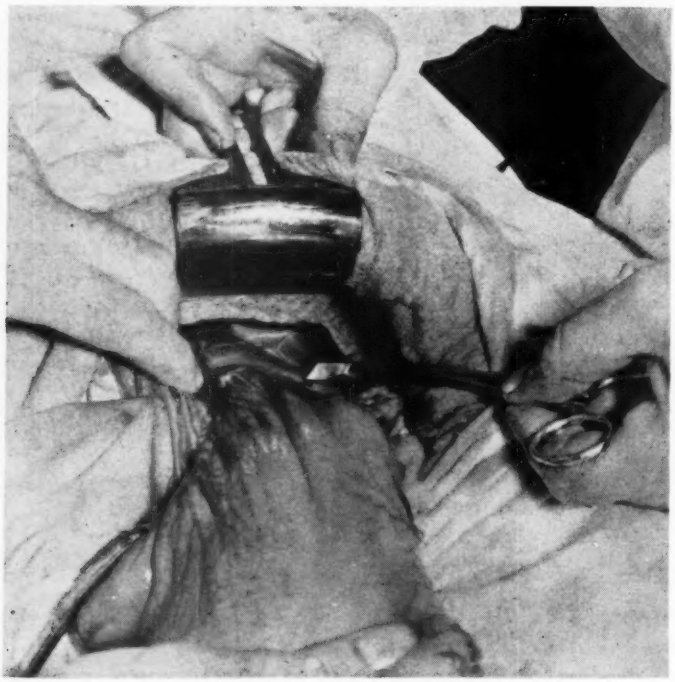

Fig. 8.—Exposure obtained by means of side incision; the forceps is pointing to the esophagogastric junction at the diaphragm.

Fig. 9.—Closed aseptic anastomosis about to begin. Anastomosis clamp on left is on duodenojejunal junction. Clamp on right is on segment of stomach remaining. The furrow at the upper end of the stomach is the diaphragmatic junction.

In both series, the animals were allowed to recover for at least one month. Their diet of table scraps, horse meat, and kibbles was reinforced with vitamins A, B, C, D, and K. After this recovery period, the second stage of the operative procedure was performed. This was the splenic vein tie maneuver, as described in the previous section. This procedure shunts the blood coming from the splenic vein into the left gastric vein and finally into the cardiac portion of the stomach and the esophageal veins, thus producing congestion and dilatation of these veins. The animals withstood this procedure well.

Another recovery period was allowed. The animals were then subjected to daily intramuscular injections of histamine-in-beeswax, and sacrificed after varying periods of time, unless the animals died spontaneously of ulcer perforation or hemorrhage.

Results: In Series I consisting of six dogs, three-quarter gastric resection and later splenic vein tie were performed. The administration of 30 mg. of histamine-in-beeswax was begun and animals were sacrificed after periods varying from three to twenty-five days. All dogs exhibited severe bleeding and there were cardioesophageal ulcers or erosions in all (Table III).

In Series II there were sixteen dogs, in all of which extensive gastric resection (90 per cent) and splenic vein tie was performed. All animals received 30 mg. of histamine-in-beeswax after the latter procedure. The animals were sacrificed in periods varying from four to forty-one days. There were two ulcers present in the series (Figs. 10 and 11). In one animal the common bile duct had been tied off accidentally (Table IV).

TABLE III. PRODUCTION OF ULCER AND/OR EROSION IN DOG WITH 75 PER CENT GASTRECTOMY AND SPLENIC TIE, FOLLOWED BY DAILY ADMINISTRATION OF 30 MG. HISTAMINE-IN-BEESWAX MIXTURE

DOG NO.	WEIGHT IN POUNDS	NUMBER OF INJECTIONS	SACRIFICED AFTER SPLENIC TIE (DAYS)	WEIGHT STOMACH REMOVED (GM.)	WEIGHT REMAINING STOMACH AFTER ANIMAL SACRIFICED	PER CENT RESECTION	RESULTS
430	35	2	3	121	42	74	Two esophageal ulcers; multiple bleeding cardiac ulcers
438	49	3	4	119	38	75	Esophageal ulcer
435	40	4	5	116	35.2	76	Multiple erosions and bleeding points at cardia and esophagus; duodenitis
441	40	16	17	110	48.3	66	Esophageal ulcer
442	33	22	23	130	34.9	79	Cardioesophageal ulcer
448	30	4	5	110	35	75	Multiple bleeding erosions at cardioesophageal junction

Number of dogs with approximately 75 per cent gastrectomy and splenic tie, 6
Number of dogs with approximately 75 per cent gastrectomy and splenic tie with ulcer and/or erosion, 6

The stomach resections in both series were estimated by weighing the resected portion at the time of the initial surgery and then weighing the portion remaining at the time the animal was sacrificed.

Clinical Case Presentations.—Surgery was performed on eight cases. The first of these patients was operated upon in February, 1945, the last during July, 1947.*

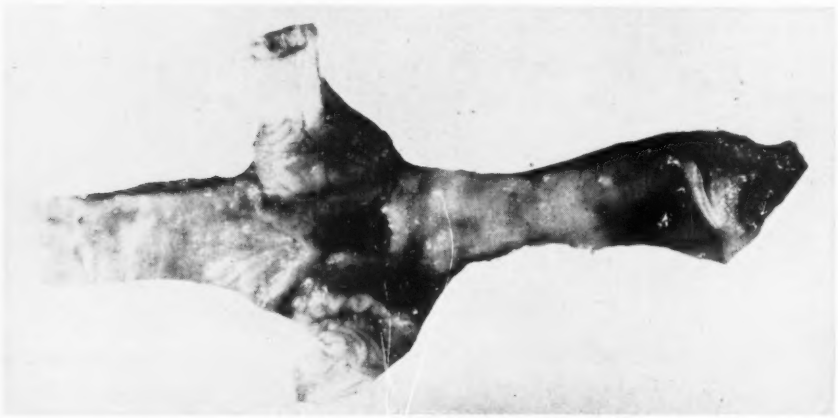

Fig. 10.—Large ulcer in a dog with extensive gastric resection (90 per cent) after ligature of left gastroepiploic and junction of left gastric and splenic veins. Histamine-in-beeswax (30 mg.) had been given for three days.

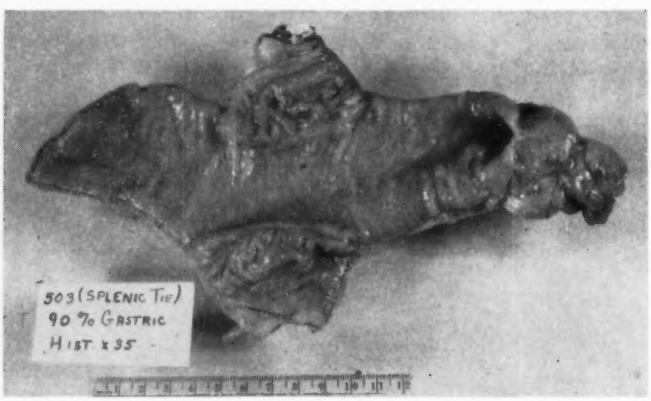

Fig. 11.—Specimen showing gastrojejunal anastomoses in a dog. An extensive gastric resection had been done and histamine-in-beeswax (30 mg.) injected for thirty-five days. Note the completely normal mucosa (Dog 503).

CASE REPORTS

Case 1 (U.H. No. 750275).—Mr. F. K., aged 59 years, was admitted to Medical Service Jan. 27, 1945, because of recurrent hematemesis first noticed in 1938. In March, 1944, esophageal varices were ligated elsewhere through a left thoracic approach. The patient bled again before leaving the hospital and there were three additional spells of hematemesis

*Dr. Owen H. Wangensteen was the surgeon in all the cases.

TABLE IV. PRODUCTION OF ULCER AND/OR EROSION IN DOG WITH EXTENSIVE GASTRECTOMY (ABOUT 90 PER CENT) AND SPLENIC VEIN TIE, FOLLOWED BY DAILY ADMINISTRATION OF 30 MG. HISTAMINE-IN-BEESWAX MIXTURE

DOG NO.	WEIGHT IN POUNDS	NUMBER OF INJECTION	SACRIFICED AFTER SPLENIC TIE (DAYS)	WEIGHT STOMACH REMOVED (GM.)	WEIGHT REMAINING STOMACH AFTER ANIMAL SACRIFICED	PER CENT RESECTION	RESULTS
436	33	3	4	110	15	88	Normal, no ulcer
447	58	13	14	170	22.4	88	Large duodenal ulcer
449	21	2	3	120	15.1	88	Normal, no ulcer
477	46	40	41	165	15	92	Normal, no ulcer
478	30	31	31	145	22.5	87	Common bile duct had been tied off accidentally; dog jaundiced, no ulcer
479	35	40	41	140	22	87	No ulcer
484	20	14	15	109	13.6	90	No ulcer
491	33	13	13	130.6	10	90	Small duodenal ulcer
494	50	40	41	157.5	20	90	No ulcer
497	28	29	30	122.6	14	90	No ulcer
498	43	40	41	162.5	15	91	No ulcer
503	51	35	36	123	22	85	No ulcer
504	36	35	36	125	12.8	91	No ulcer
507	33	30	31	156	19.2	89	No ulcer

afterward. A carcinoma of the right bronchus close to the carina also had been demonstrated since the ligation of the esophageal varices. The hemoglobin, when the patient was first seen in the medical outpatient department, was 7.52 Gm. per cent. On Feb. 8, 1945, a few days after admission to the medical service, the hemoglobin was 9 Gm. On Feb. 9, 1945, the patient began bleeding again and 500 c.c. of blood was given daily by the medical service over a period of five days, a total of 2,500 c.c. being given. At the end of this time, the hemoglobin was 7 Gm. After transfer to the surgery department, one liter of blood was given daily for nine days including the day of operation, the hemoglobin rising slowly to 12.3 Gm. per cent. Blood was demonstrated constantly in the stool. Gastric analysis without histamine showed a maximum of 27 degrees free acid and a total of 39 per cent. A bronchoscopy done on Feb. 5, 1945, showed a squamous-cell carcinoma to be present in the right main bronchus. The x-ray findings of the chest were consistent with a carcinoma of the right lung. Liver function studies were normal. There was no ascites.

On Feb. 23, 1945, a 90 per cent gastric resection was done on the thesis that an increased portal pressure produced a passive congestion of the gastric mucous membrane, which, in the presence of free hydrochloric acid, made the mucous membrane more vulnerable to acid-peptic digestion. In other words, it is believed that bleeding from the esophageal or gastric varices is primarily an erosion rather than a bursting process. The blood loss in the operation was 1,190 Gm.

The spleen was also large and was removed. It weighed 870 grams. The removed stomach weighed 225 grams. The portal and splenic veins were both large and their walls, as in an atheromatous process, were somewhat thick. The portal pressure was 25 cm. of saline solution. The liver appeared normal. The operative diagnosis was, therefore, primary thrombophlebitis of the portal and splenic veins.

The microscopic study on the spleen showed a condition of fibrosis consistent with the diagnosis of Banti's disease. The liver was normal microscopically. There were no areas of atrophy in the gastric mucosa and there was a moderate amount of interstitial antral gastritis present, as is commonly observed in duodenal ulcer.

The patient did well after operation and the hemoglobin promptly rose to 14 Gm. There has been no further evidence of bleeding. The patient was dismissed on March 6, eleven days after operation. On March 27, he returned for excision of the right lung

which was done on April 4. The lesion in the bronchus was quite near the carina, necessitating amputation close to the bifurcation of the trachea. The lung was universally adherent but was excised without difficulty. The lung weighed 620 grams. There was no tumor in the removed lymph nodes. The tumor in the bronchus extended over a distance of 3 cm. and practically occluded the bronchus. The biopsy diagnosis of squamous-cell carcinoma was confirmed.

A transfusion of 1,000 c.c. of blood was given for this operation, the blood loss in operation being 1,450 Gm. This was the only transfusion the patient received following gastric resection on that hospital admission. The patient did very well after operation. He manifested very little operative reaction and was dismissed on April 15, eleven days after operation. The hemoglobin on April 11 was 10.5 Gm.

On Sept. 19, 1945, the patient was readmitted with a history of melena and hematemesis of one week's duration. He was transferred and treated with a continuous drip of a high protein diet and Amphojel. He responded nicely and was discharged to return at a later date for further resection.

On Dec. 8, 1945, the patient was readmitted to the service with generalized anasarca and 8,500 c.c. of fluid were obtained by abdominal paracentesis. Two days after this admission, he suddenly had a severe hematemesis and died in spite of vigorous measures of therapy.

Post-mortem revealed the presence of esophageal varices that could be demonstrated but with no demonstrable rupture. A thrombus was present in the portal vein completely occluding it. The liver appeared normal.

CASE 2 (U.H. No. 744513).—Baby boy, R. C., was 3 years of age. On July 28, 1944, splenectomy was done because of repeated hematemesis and melena. The removed spleen weighed 170 grams. The liver appeared nodular and cirrhotic. A piece removed for biopsy showed definite cirrhosis microscopically. The patient was dismissed Aug. 8, 1944. On April 11, 1945, the parents brought him back because of melena. In the hospital, vomiting of blood occurred necessitating transfusions for shock. The hemoglobin, which had been 13.4 Gm. on the first admission fell to 5.6 Gm. Under daily transfusions of 250 to 500 c.c. of blood, the hemoglobin rose to 10.7 Gm. on April 23, 1945, at which time a 98 per cent gastric resection was done. The liver appeared somewhat more nodular than at the last operation. The portal venous pressure was not determined. A specimen withdrawn prior to operation for gastric analysis contained largely blood. No transfusions were given after operation and the hemoglobin rose to 14.2 Gm. Blood disappeared from the stool and when the patient left the hospital on May 6, 1945, he was eating well.

He was readmitted on Sept. 3, 1947, with a history of a tarry stool that morning. Hemoglobin at the time of admission was 8.4 Gm. During his stay at the hospital of nine days, no tarry stools nor hematemesis was noted. He was transfused up and put on a diet of puréed foods. No other therapy was instituted. The patient progressed nicely and was discharged on Sept. 9, 1947. Prothrombin time at discharge was elevated slightly.

CASE 3 (U.H. No. 622258).—Mrs. E. H., aged 27 years, was admitted May 21, 1945, because of hematemesis, melena, and a feeling of faintness. Blood has been present persistently in the stool since May 19, 1945. The hemoglobin was 8.8 Gm. In 1938, this patient's spleen was removed because of recurrent hematemesis and melena. There were a number of accessory spleneculi found. The diagnosis was thrombophlebitis of the splenic vein. The liver appeared normal. There had been no recurrence of hematemesis or melena until just before admission. There was no ascites; liver function tests were normal. The patient had free hydrochloric acid in all of the four samples without histamine, the highest value being 36 degrees. Three transfusions of blood were given and the hemoglobin rose to 11.7 Gm. on the day of operation. On June 4, 1945, a 95 per cent gastric resection was done. The liver appeared normal; no surviving splenic tissue was observed. The portal venous pressure measured in an omental vein was 49 cm. of saline solution. The mesenteric veins appeared full and were very prominent. The suspensory ligaments of the liver were

extremely vascular and thick, making dissection difficult. The omentum was universally adherent in the upper right quadrant and contained prominent veins. The fundic portion of the stomach was intimately adherent to the left diaphragm and pancreas over a wide extent. The removed stomach weighed only 114 grams. There was little operative reaction. The patient convalesced nicely from the procedure and was dismissed from the hospital seven days after operation. She is well with no hemorrhage two years after surgery.

CASE 4 (U.H. No. 764840).—C. G., a young man 17 years of age, had been admitted to the hospital on June 3, 1947, with a history of repeated attacks of tarry stools for two days previous to admission. At the age of 7 a splenectomy for Banti's disease had been performed. There had been two previous admissions at which time a liver biopsy with a normal pathologic report, and treatment with dicumarol had been instituted. The presumptive diagnosis of thrombophlebitis of the portal vein had been made.

On two occasions gastric analysis had revealed 24° and 38° of free acid on the fasting sample. Liver function studies done previously revealed no extraordinary deviation from normal.

This admission was occasioned by a severe hematemesis of 1½ liters of blood while waiting for admission. This process, plus melena, characterized most of his entire stay in the hospital this time. A total of 63 bottles of blood amounting to about 30,000 c.c. was given during a period of the first sixteen days. In addition nasal tube feeding, topical thrombin, Amphojel, and various other agents were used to stop the bleeding and to control the stomach acids.

Bleeding and clotting times, prothrombin determinations, and platelet counts during this period of time were normal. Hemoglobin determinations varied between 3.4 and 12 Gm.

Following this therapy the patient improved. He still remained febrile for a while and surgery was contemplated only at a time when he was afebrile for a period.

On July 7, 1947, a total gastrectomy with esophagojejunostomy was done. The portal pressure measured 38 cm. of water. All the ligamentous attachments to the stomach were heavy. The operation went without event. At first a 95 per cent resection was to be done, however, the following operative note of Dr. Wangensteen is pertinent: "My first attempt was to do about a 95 per cent resection. Owing, however, to the circumstance that the tethering of the stomach was unusually close to the posterior abdominal wall, I finally had to give it up. I therefore decided upon total gastrectomy which in this case was decidedly easier because we were able to dissect the stomach off the posterior abdominal wall. The strange part of it was that, whereas I thought I was doing about a 95 per cent resection at first, the first gastric fragment which went out weighed 265 grams. The remaining fragment, which I thought represented only five per cent of the entire stomach weighed 27 grams, representing, therefore, more than 10 per cent of the entire gastric weight."

The postoperative course was entirely uneventful and the patient left the hospital fourteen days after surgery. When last seen seven months after surgery, the patient was feeling well and eating four meals a day. His hemoglobin was 14.8 Gm.

CASE 5 (U.H. No. 749135).—Mrs. M. V., a 62-year-old white woman, had had periodic melena over a period of years. On admission the hemoglobin was 4.5 Gm. Fifty-nine per cent free acid was present in the gastric juice. Ascites and diminution of liver function was present. A diagnosis of cirrhosis with varices was made. A 90 per cent gastrectomy and splenectomy was done. A subphrenic abscess developed postoperatively and the patient died.

CASE 6 (U.H. No. 670905).—Miss B. P., a 25-year-old white woman, had had multiple bouts of hematemesis. Ascites was present with only fair liver function. Hemoglobin on entry was 5.4 Gm. Twenty per cent of free acid was present. Diagnosis of cirrhosis with varices was made. A 95 per cent gastrectomy and splenectomy was done. Liver was definitely cirrhotic. The postoperative course was downhill and she died due to marked liver deficiency.

CASE 7 (U.H. No. 758344).—Miss L. M., a 48-year-old white woman, was admitted because of recurrent attacks of hematemesis and melena. Gastric analysis revealed 36 per cent free acid. Liver function studies revealed definite diminution of liver function. A diagnosis of cirrhosis with varices was made. A splenectomy and total gastrectomy were done, but the patient died during the postoperative course of acute liver necrosis.

CASE 8 (U.H. No. 778775).—Mrs. E. M., a 63-year-old white woman, was admitted with a history of multiple bouts of hematemesis. The liver was enlarged and biopsy revealed cirrhosis. Free acid was present in the gastric juice. Ascites was also present. A 96 per cent gastrectomy and splenectomy was done. A subphrenic abscess developed and in spite of drainage she died thirty-five days postoperatively of a suppurative pylephlebitis of the portal vein.

Interpretation and Discussion.—The acid-peptic factor may be considered as important a factor in the bleeding of esophageal varices as the hydrostatic factor. Experimentally, a 90 per cent resection offers real but no absolute protection against the histamine-provoked ulcer in the presence of portal hypertension. Clinically, this was borne out in Case 1. One must do something akin to a total gastrectomy to afford absolute protection.*

Another factor in the selection of patients for extensive gastric resection is the liver function status. It has been clinically borne out that patients with poor liver function do not tolerate major surgery as well as other patients. Three out of the four who died in the postoperative period in our series showed a definite diminution of liver function with cirrhosis (Cases 5, 6, and 7). Note must also be made that all of the four patients on whom follow-up studies were done had good liver function (Cases 1, 2, 3, and 4). One of these patients (Case 2) had cirrhosis. Careful evaluation and preparation must therefore be made. However, it must be remembered before one deters from the surgical management of the bleeding in cirrhoses, that Eppinger (1937) has indicated that a fairly large number of patients with cirrhoses of the liver die of hemorrhage before ascites or liver insufficiency supervene (16 per cent).

Moreover, those cases of bleeding that are associated with congestive splenomegaly without cirrhosis must be seriously considered as amenable to surgery. It is not infrequent that bleeding from the stomach is overlooked in these cases. The presence of minute erosions in the stomach may cause serious blood loss (Bortz, 1932). The occurrence of ulcer and/or erosion of the stomach in cirrhosis was mentioned by Eppinger (1937), and Smith and Farber (1935) indicated them in their protocols on thrombophlebitis of splenic vein on bleeding from gastric mucosal veins of a serious nature.

It might be argued that a successful portacaval shunt would have the theoretical advantage over gastrectomy with regard to the problem of ascites. The former would, in addition to shunting the portal blood into the caval system, also attack the problem of ascites. However, in addition to portal constriction as a cause, ascites, colloid osmotic blood changes, and vascular permeability changes are considered as causes. Butt, Snell, and Keys (1939) measured the colloid osmotic pressure of the serum in cirrhosis and found it reduced to one-

*Since submission of this paper for publication, Dr. Hay, Chief of Surgery at Veterans Hospital, Minneapolis, has performed a total gastrectomy in a patient with Banti's disease and hematemesis with an excellent result.

half the normal value (200 to 250 mm. of water, normal being 375 mm.). Since in cirrhosis the portal pressure may rise up to 500 mm. of water, it is probable that a favoring of transudation occurs. Of the seven cases of cirrhosis presented by Blakemore (1946) in which ascites was present, four required paracentesis postoperatively.

Wangensteen first suggested virtual total gastric resection (95 to 98 per cent) in 1945. More recently, Phemister and Humphreys (1947) have performed total gastrectomy and esophagogastric resection for the bleeding due to Banti's syndrome. Dilated veins in the submucosa of the fundus of the stomach which in one case communicated with dilated veins of the mucosa are shown. An examination of the microscopic sections of the cases followed postoperatively in our clinic reveals dilated submucosa and mucosal vessels also. However, this may be a normal occurrence during surgery of the stomach. It, indeed, would seem surprising that the acid-peptic factors of the stomach could not easily cause digestion of the impaired mucosa over these. However, patients with bleeding from the upper reaches of the alimentary tract who have hepatic cirrhosis on Banti's syndrome appear to have generous amounts of free hydrochloric acid in their gastric juice.

It perhaps should be indicated, too, that gastric resection in a patient with portal hypertension may be a more difficult operation than in a patient with ulcer. The omenta and tethering membranes and ligaments of the stomach are thickened up, owing to the new vessel proliferation. Dissection, in consequence may be difficult. When, on exploration, the liver appears normal as it usually does in Banti's disease, measurement of the venous pressure is important. In thrombophlebitis of the portal vein the venous pressure will be up, whereas in bleeding from a silent, nonpalpable gastric erosion, the venous pressure will be normal. For the latter type of case, the conventional 75 per cent gastric resection is adequate; for the portal hypertension, at least a 95 per cent resection should be done. Moreover, improvements in technique suggest that total gastric excision now too can be done with risks not far out of line with subtotal resection.

More recently we have employed the principle of air-vent suction drainage in our cases of total gastrectomy with splenectomy. This drain is attached to suction created by a small flea power motor which runs continuously. This has been of definite aid in the convalescence of patients with total gastrectomy and splenectomy. It is well known that drainage following splenectomy is usually present. This has been thought to be due to injury of lymphatics and small vessels in the bed of the spleen and diaphragm. However, in a recent case of total gastrectomy and splenectomy for carcinoma of the stomach, the fluid aspirated by means of air-vent suction proved to be almost pure pancreatic juice. Either injury to the tail of the pancreas in the vicinity of the hilum of the spleen or the presence of anomalous pancreatic ducts extending to the hilum must therefore be seriously considered and air-vent suction employed.

SUMMARY

The problem of bleeding associated with portal hypertension has been reviewed and investigated. Heretofore, particular stress has been placed on the

hydrostatic factor as the important one in bleeding from esophageal varices. Another item, that is, that of the acid-peptic digestive factor is considered.

By means of a long subcostal incision it was possible to do extensive gastric resections (90 per cent) on fourteen dogs. Portal hypertension was then produced and the animals were subjected to histamine-in-beeswax. The abeting influence of portal hypertension on the ulcer diathesis is shown by the fact that in two of the dogs with extensive gastric resection (90 per cent) and all of a series of dogs (six) with a three-quarter resection ulcers and/or erosions were found.

Extensive gastric resection has been performed on eight patients. Follow-up study was done on four of these patients postoperatively. The remainder died in the immediate postoperative period.

One of the former patients died recently of hemorrhage. A 90 per cent gastrectomy had been done. Possibly a more extensive resection was in order, as experimentally a 90 per cent resection offers real but not absolute protection against histamine-provoked ulcer in the presence of hypertension. The remaining three patients were doing well up to the periods of two years (one 95 per cent; one 98 per cent; one total gastrectomy).

We have come to learn that selection of patients for extensive gastric resection is a sine qua non in portal hypertension. Of the four patients who died in the immediate postoperative phase, three had diminished liver function. Blakemore (1946) came to a similar conclusion in his selection of patients for portacaval shunt operations. The presence of ascites need not deter one from surgery, for Eppinger (1937) has shown that this may actually precede hepatic insufficiency by a long time.

In addition to removing the acid-peptic digestive juices which are present in generous amounts in patients with portal hypertension, extensive gastrectomy will isolate the portal from the caval system, and decrease the total inflow into the portal vein. That shunting of the portal to the caval system by means of a splenic-renal vein anastomosis does not decrease the portal pressure to normal is evidenced by Blakemore's report (1946). However, it may be a step in the right direction.

Surgery is definitely indicated in those cases of extrahepatic portal block. (Thrombophlebitis of the portal vein, cavernomatous transformation, stricture, etc.) Gastrectomy may be used as a procedure of choice, as in the Blakemore procedure the thrombus may extend and compromise the return of blood from the small intestine.

W. J. Mayo (1924) pointed out the efficacy of splenectomy in relieving the symptoms of cirrhosis which was classified by him as the splenic type occurring in the late stages of splenic anemia. He believed it unwise for such extensive surgery to be attempted in the type classified as gastrointestinal, for the liver was usually badly damaged, and surgery would not be tolerated. More recently Blakemore and Lord (1945) suggested splenectomy for those cases of splenomegaly due to thrombosis of the splenic vein distal to the entrance of the left gastric vein, if it enters there.

The use of air-vent suction in cases of extensive gastric resection plus splenectomy has proved itself very helpful in minimizing postoperative complications. Its placement in the bed of the spleen in a case of total gastrectomy and splenectomy for carcinoma of the stomach has shown that the presence of pancreatic drainage must be considered.

Finally, it may be said that all operative procedures directed at correcting hemorrhage in hepatic cirrhosis are essentially palliative in nature, for we do not know how to arrest cirrhosis itself. Yet life may be prolonged through operative procedures which lessen the tendency to hemorrhage.

CONCLUSIONS

1. Portal or splenic vein obstruction abets the ulcer diathesis.

2. Extensive (90 per cent) gastric resection affords real but not absolute protection against the histamine-provoked ulcer, in the presence of portal hypertension.

3. A 75 per cent gastric resection affords no protection against histamine-provoked ulcer in the presence of portal hypertension.

4. Gastrointestinal bleeding of portal vein obstruction may be corrected in patients by a 95 to 98 per cent resection which reduces materially the capacity of the stomach to secrete. The case records of eight patients in whom such extensive resections were carried out are presented.

5. Bleeding within the stomach may occur as a result of erosions of the dilated veins of the stomach, and gastric resection is indicated as a therapeutic measure in many such instances.

6. It is suggested that the portal inflow may be decreased by removal of the stomach and spleen.

7. Isolation of the portal and caval systems may be accomplished by extensive gastric resection.

8. Air-vent suction drainage aids materially in the recovery of patients with total gastrectomy and splenectomy.

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